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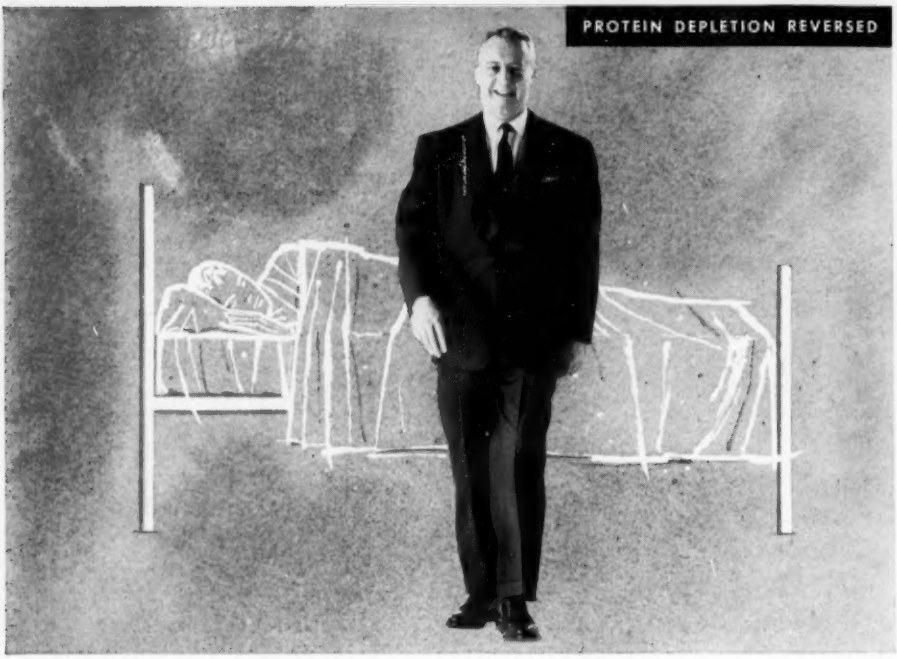

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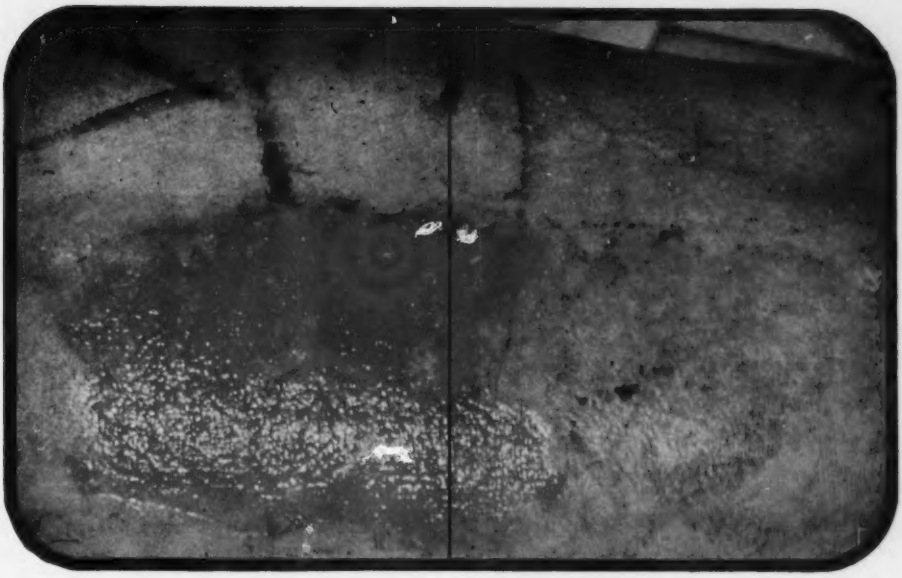

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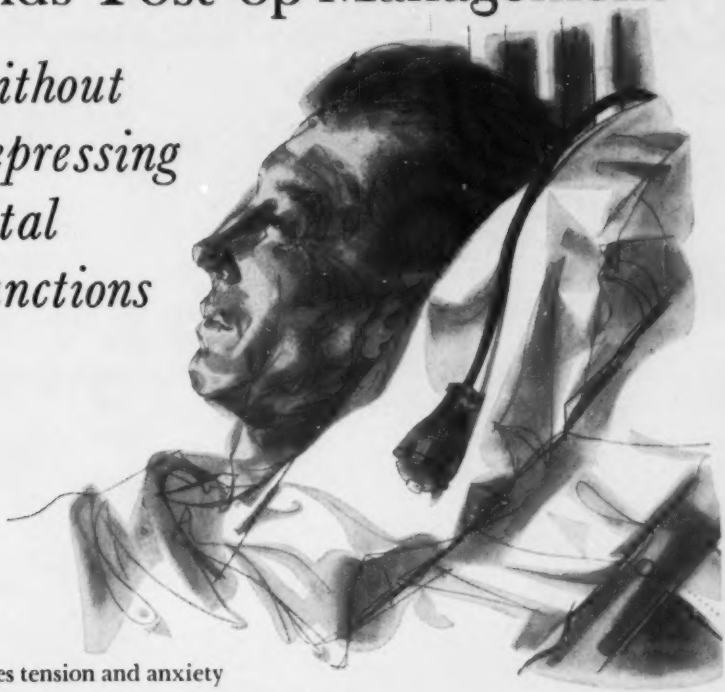

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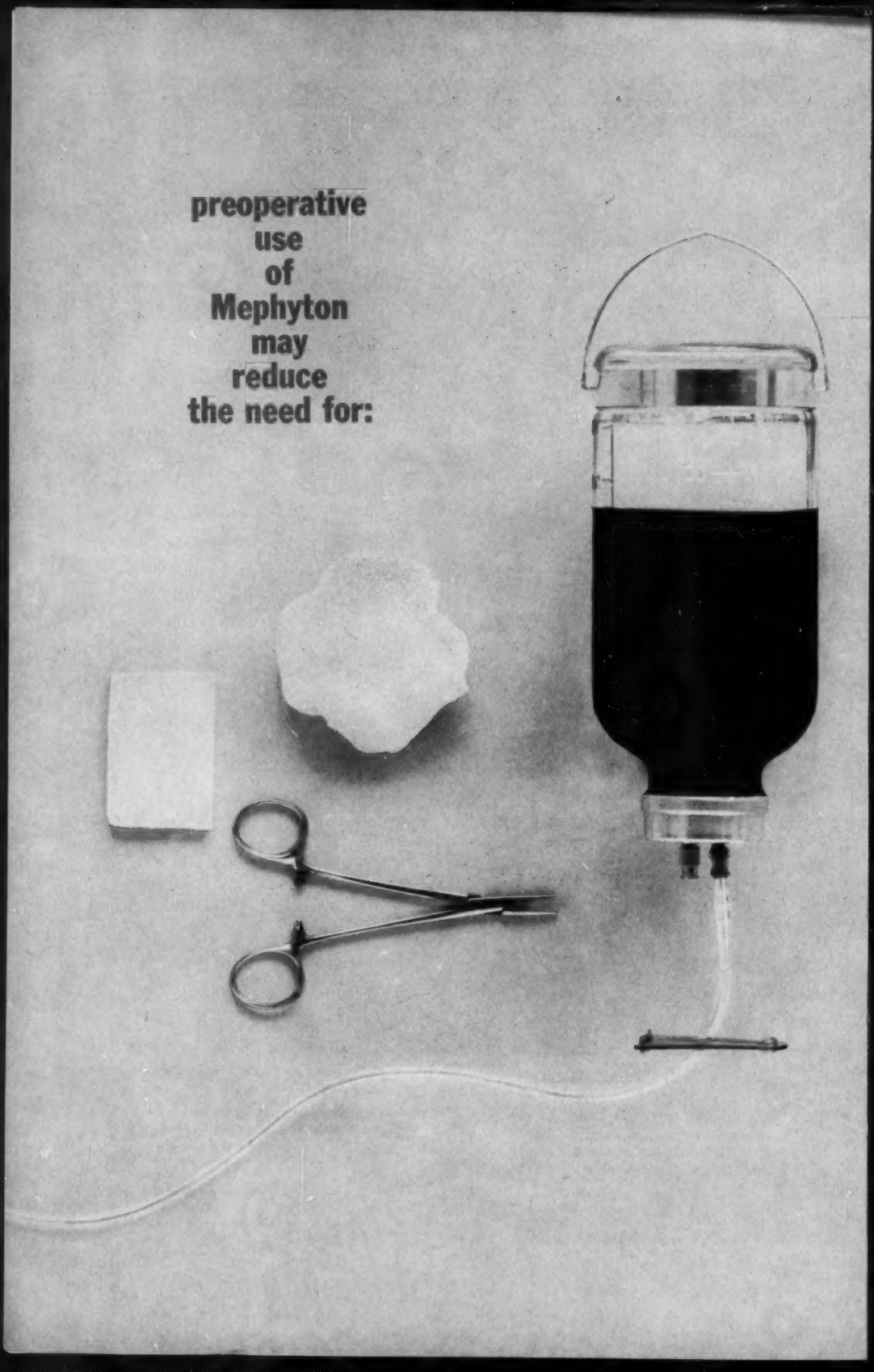

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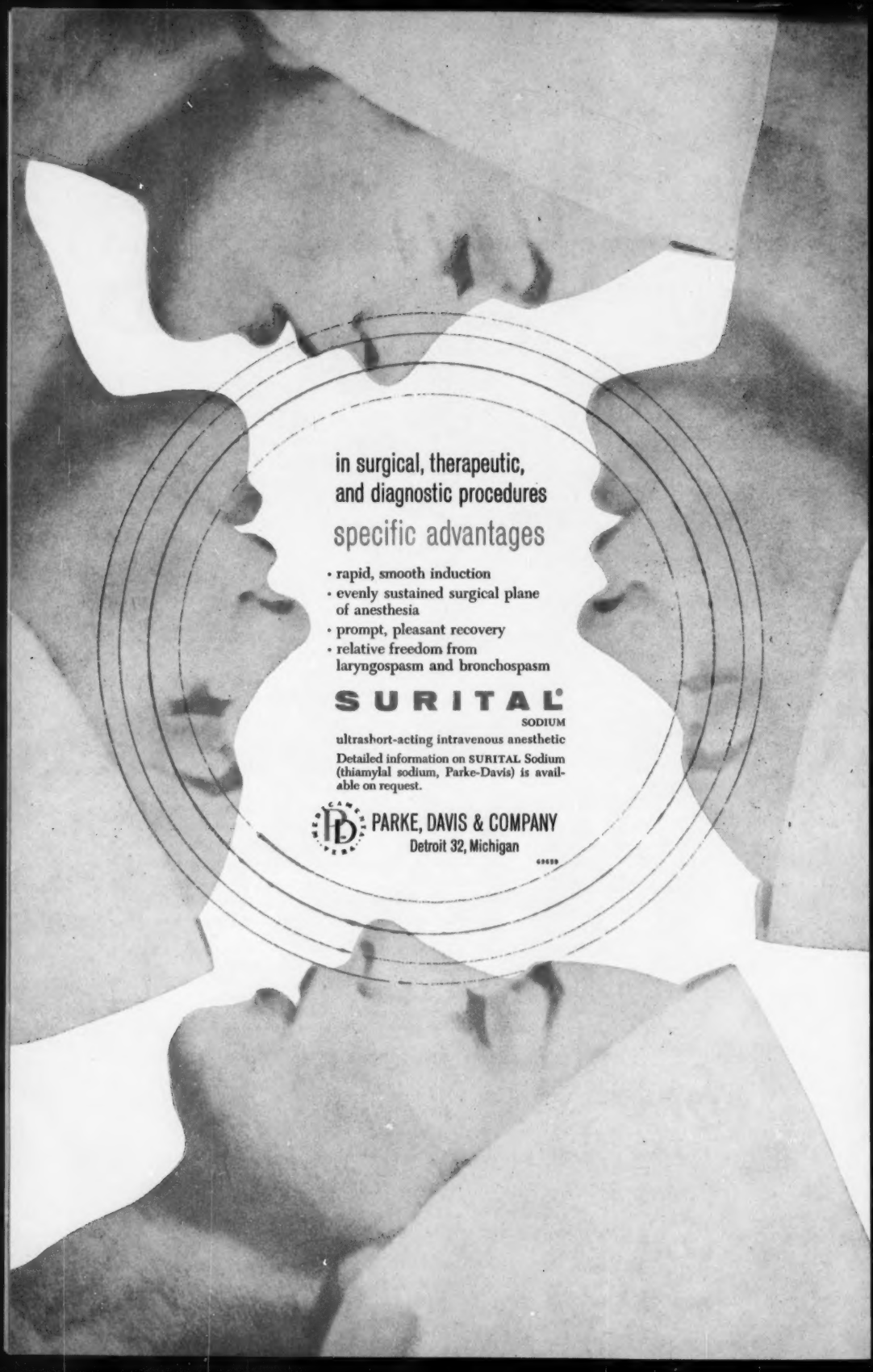
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The Effect of Antiperistaltic Bowel Segments on Intestinal Emptying Time

JOHN M. HAMMER, M.D.; PATRICK H. SEAY, Ph.D.; RICHARD L. JOHNSTON, D.V.M., Kalamazoo, Mich.; EDWARD J. HILL, M.D.; FRANK H. PRUST, M.D., and RUTH J. CAMPBELL, M.D., Detroit

In the *Johns Hopkins Report* in 1896, Mall [1] stated that the reversal of an intestinal segment was fatal to an animal. This statement has appeared unchallenged in physiology textbooks for many years, although investigators [2,3] have found that it is not necessarily true. When Hammer et al.[4] reversed the entire duodenum in a series of dogs in 1952, the animals survived. It was found that they developed a marked delay in the emptying time of the stomach and that both the reversed segment of duodenum and the stomach dilated. After approximately six months many of the animals in the series developed jejunal ulcers at the site of the gastrojejunostomy. Further studies by Hammer et al.[5,6] showed that animals could survive the removal of 80% of the small intestine if a short segment was reversed. However, if a segment was not reversed, the animals usually died of starvation within 90 days.

Material

Six series of animals have been experimented on: (1) Two-thirds of the small bowel was removed; no segment was reversed, and the animals were fed an ordinary laboratory diet; (2) 75% of the small bowel was removed; no segment was reversed, and the animals were fed an ordinary laboratory diet; (3) 80% of the small bowel was removed; no segment was reversed, and the animals were fed an ordinary laboratory diet; (4) 80% of the small bowel was removed; no segment was reversed, and methscopolamine (Pamine) bromide (epoxytropine tropate methylbromide) was added to the diet as a drug control; (5) 80% of the small bowel was removed; a short segment was reversed, and the animals were fed an ordinary laboratory diet; (6) 90% of the small bowel was removed; a segment was reversed, and the animals were fed an ordinary laboratory diet.

Submitted for publication April 3, 1959.

Presented at the Seventh Annual Meeting of the Michigan Chapter of the American College of Surgeons, Detroit, March 10, 1959.

Procedure

Adult beagles weighing 20-25 lb. were used in the experiments. Beginning 48 hours prior to surgery, 1,000,000 units of penicillin was administered intramuscularly and 0.5 gm. of neomycin was administered orally twice a day. The animals were starved except for water for 24 hours preoperatively, then anesthetized with veterinary pentobarbital (Nembutal) sodium (Abbott) given intravenously, 1 ml. (50 mg.) per 5 lb. (2.3 kg.) of body weight. The abdomen was shaved, prepared with mercocresols (Mercresin tincture) and draped with clean nonsterile towels. The peritoneal cavity was entered by a midline abdominal incision extending laterally to the penis. The small bowel from the ileocecal valve region to the ligament of Treitz was brought out on the abdominal wall. As the bowel in a living animal cannot be measured accurately, the length and percentages were calculated on the basis of the average small bowel in a 20-25 lb. dog under anesthesia measuring 12 to 13 hemostats (7 in.) in length along the antimesenteric border. Approximately 10 hemostat lengths were considered to equal 80% of the small bowel. This measured segment was resected, using open anastomoses.

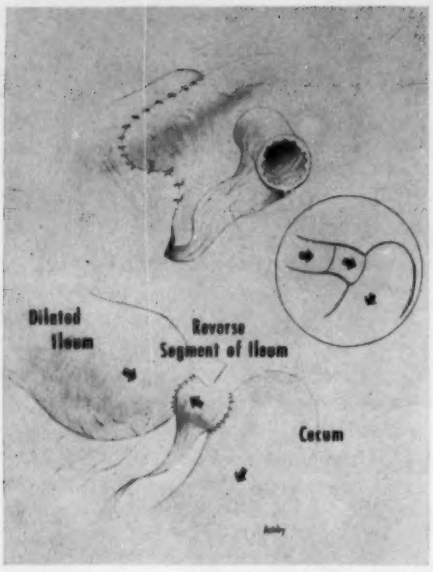

Fig. 1.—This illustration demonstrates the effect of an isolated bowel segment inserted into the intestinal tract of an animal. If the segment is inserted in an antiperistaltic manner, it produces a marked dilatation of the intestine proximal to the segment; this is accompanied by a marked delay in emptying time. If the segment is inserted in an isoperistaltic manner, there is no dilatation or delay in the emptying time of the bowel.

The distal 2 in. of the remaining jejunum or ileum was selected for reversal on the basis of being anatomically available. The smaller branches of blood vessels from the intestine were clamped, divided, and ligated as they were followed through the arcuate arteries of the main branch coming off the mesentery, thus leaving a segment of bowel with a long mesentery which could be freely manipulated without interfering with the blood supply. This segment was clamped, ligated, and divided, and after being reversed was anastomosed in an oblique manner proximally to the jejunum and distally to the cecum (Fig. 1). A two-layer running silk technique was used for the anastomoses. The oblique anastomosis was used since we had found in previous work[4,5] that it eliminated difficulties encountered with end-to-end or side-to-side anastomoses. When an end-to-end anastomosis had been used the animals died of high intestinal obstructions. The animals in which a side-to-side anastomosis was used often developed huge pouches in the proximal line stump which became filled with bezoars from wood shavings in the cages. The bezoars became palpable as they grew larger, and the animals sometimes developed bowel obstructions when the stoma was obstructed by these bezoars.

Comment

The three animals in the series in which two-thirds of the small bowel was removed were able to maintain themselves on an ordinary laboratory diet with no weight loss or other ill effects, but the three animals in which 75% of the small bowel was removed developed diarrhea and died of starvation in three months (Table 1).

Of the three series of animals in which 80% of the small bowel was removed, the three animals which did not have a bowel segment reversed and which received no methscopolamine all died of cachexia within a period of three months.

The second series of animals in which 80% of the small bowel was removed had no segment reversed, but were given 2.5 mg. of methscopolamine per kilogram of body weight twice a day in their regular diet and were used as drug controls. These six animals maintained themselves with the medication, but two animals died when taken

TABLE 1.—*Effect of Insertion of Bowel Segment into Intestinal Tract*

	Per Cent of Small Bowel Removed					
	66%	75%	80%	80%	80%	90%
No. in series	3	3	3	6	6	6
Segment reversed	No	No	No	No	Yes	Yes
Diet	Normal	Normal	Normal	Methscopolamine added	Normal	Normal
Deaths	--	3	3	2	--	3
Cause of death	--	3 mo. Starvation	3 mo. Cachexia		--	6 mo. Cachexia
Living	3	--	--	4	6	3
Survival time	2 yr.	--	--	2 yr.	2 yr.	2 yr.

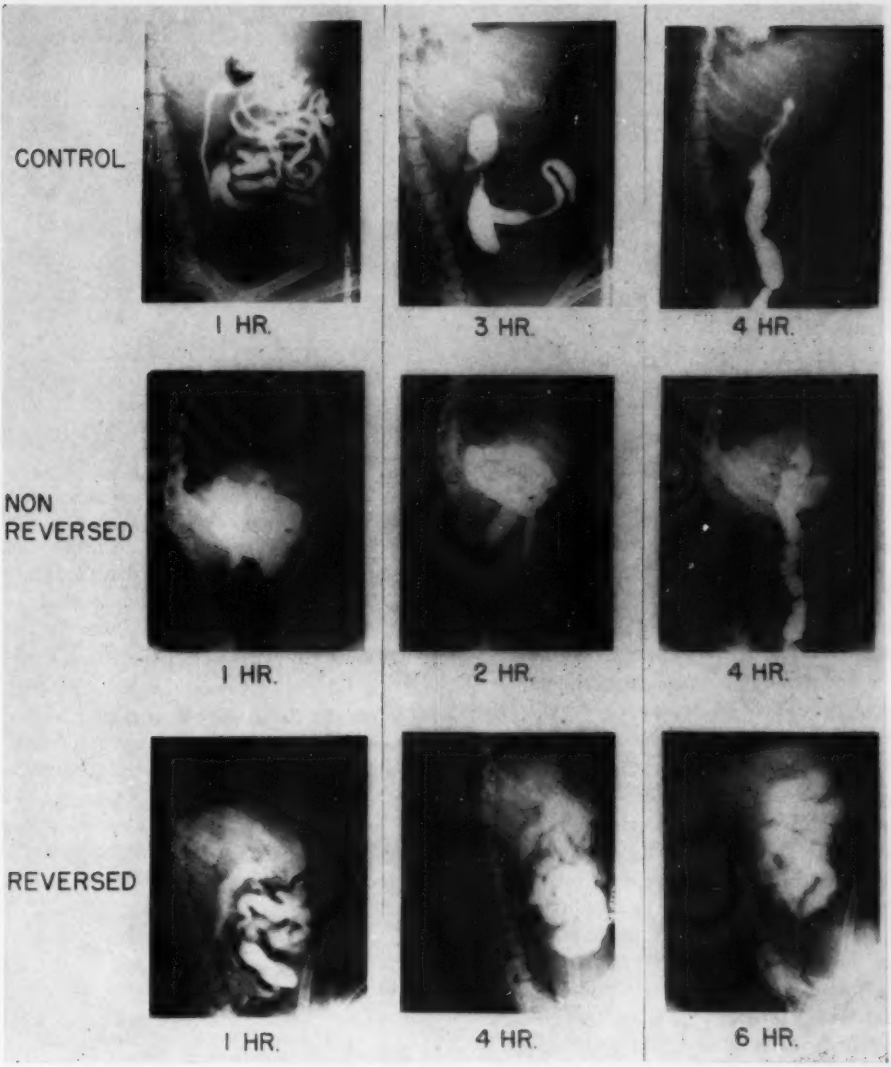

Fig. 2.—This series of x-rays demonstrates the passage of barium through the intestinal tract of a dog. In the control animal most of the barium is visible in the loops of small intestine after one hour. After three hours the small intestine is practically empty with most of the barium located in the terminal ileum and ascending and transverse colon. After four hours the barium is in the descending colon. In the animal with most of the small bowel removed and a segment inserted in an isoperistaltic manner (not reversed), the barium appears to pass directly from the stomach through the bowel as in the control animal. In the animal in which a segment of distal small intestine is inserted in an antiperistaltic manner (reversed) there is still a considerable amount of barium left in the stomach after an hour, although a small amount has entered the small bowel. After four hours barium remains in the stomach and small bowel with none in the colon. After six hours most of the barium still remains in the small bowel proximal to the reversed segment.

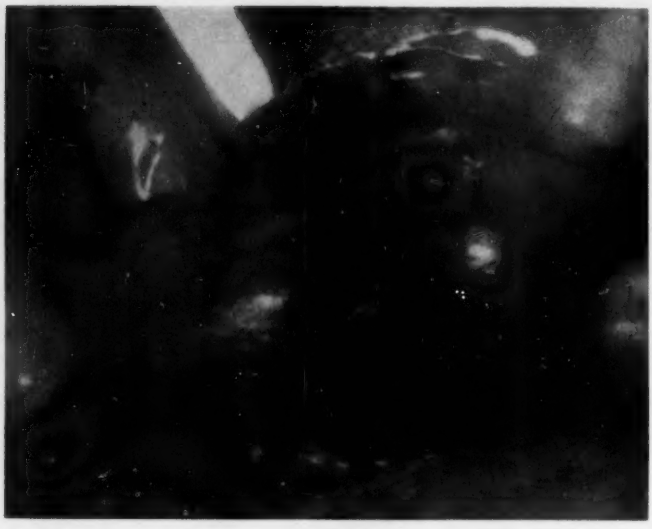

Fig. 3. — This picture shows the segment in an animal approximately one year postoperatively at a second laparotomy. The dog's cecum is in the operator's gloved right hand. The point of the scissors is at the narrowed reversed segment.

off the methscopolamine. The remaining animals have developed some side-effects after prolonged administration of the drug. They have difficulty urinating, tend to develop urinary infections, develop extreme thirst, and are prone to infections of the mucous membranes (conjunctivitis). Some have developed impactions or bezoars with resulting intestinal obstructions.

The six animals which had 80% of the small bowel removed and a segment reversed have lived and maintained their weight for over two years. X-rays and laparotomies have been done at intervals on these animals. The x-rays have revealed a marked dilatation of the stomach, duodenum, and jejunum above the reversed segment and a marked delay in the emptying time of the bowel, sufficient to allow these animals to absorb food and maintain weight (Fig. 2). At laparotomy all the intestine above the reversed segment, including the stomach, duodenum, and proximal jejunum, was dilated and somewhat hypertrophied. The reversed segment had narrowed down to approximately 1 cm. in length with a lumen of less than 1 cm. in diameter, producing a physiological valve (Fig. 3). This is probably the reason for the delay in the emptying time of the bowel and the maintenance of the dogs' weight; the food was held there long enough to be absorbed and was in contact with the digestive enzymes of the stomach, pancreas, and the liver. The blood chemistry was normal (Table 2) and the stools were grossly normal.

Three of the six animals in the series with 90% of the small bowel removed and a segment reversed died of cachexia within six months. The remaining three animals have maintained weight and are doing well after more than two years. They have the same x-ray, laparotomy, and blood chemistry findings as the series of animals with

TABLE 2.—*Blood Chemistry of Dogs Before and After Surgery*

	Before Surgery (Normal)	1 Week After Surgery	6 Months After Surgery	1 Year After Surgery
Total proteins	5.96	5.84	4.90	5.50
Albumin	4.39	4.37	3.60	4.17
Globulin	1.57	1.47	1.30	1.43
A/G ratio	2.8/1	2.97/1	2.80/1	2.79/1
Serum chlorides	405.6	420.	575.	575.
Serum sodium	284.3	285.	309.	309.
Serum potassium	10.4	10.1	15.6	15.6
Nonprotein nitrogen	43.5	44.1	56.1	54.0
Carbon dioxide	45.8	43.8	43.8	44.0

All values are expressed in mg. per 100 cc.

80% of the small bowel removed and a segment reversed.

It is of interest to note the possibilities of such a procedure in human mesenteric thrombosis. Some of these mesenteric thromboses involve 80% to 90% of the small bowel and often part of the large bowel. Such patients, even if they survive their definitive surgery, usually die within a matter of months of diarrhea, starvation, and cachexia. Conceivably a reversed segment in such patients might produce a delay in the emptying time of the human intestine as it has in dogs. With intact digestive enzymes in the stomach, liver, and pancreas and the delayed emptying time, maintenance of weight might be achieved.

Conclusions

Animals with 80%-90% of the small bowel removed survive and maintain weight if 1 to 2 in. of the distal segment of remaining bowel is reversed and reinserted into the intestine in an antiperistaltic manner.

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A Study of Reinforced Ivalon as Prosthetic Material for Arterial Replacement

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Polyvinyl formalinized (Ivalon) sponge has been tested as prosthetic material by several groups, with some variation in findings.[1,6,7,9] It has unique and desirable characteristics, which include (1) inherent ability to hold a shape which adds greatly to the ease of placement and decreases the likelihood of wrinkles; (2) ease in fashioning into any desired shape by heating while molded; (3) a high degree of porosity which allows rapid and secure fibroblastic penetration—conversely, the degree of porosity can be controlled at will by varying the compression used during molding; (4) ability to fuse itself together, without seams. In experimental and clinical use as an arterial replacement it has seemed to have approximately the same tendency to thrombosis as other materials; however, it has had the serious disadvantage of low inherent strength, and the incidence of aneurysm formation and rupture has been rather high, especially when it is used in the thorax.[2,4]

It was considered that reinforcement of the sponge might correct the lack of strength while retaining its good features. Accordingly, a method of construction with reinforcement was devised and an experimental study carried out using this material as an arterial replacement. In addition to the primary objective of this study, observations were made on the effect of host-graft disproportion, effect of diameter, and effect of porosity.

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Methods

Construction of Prostheses.—Blocks of Ivalon sponge were sliced into thin (1-2 mm.) sheets. These sheets were wrapped on glass rods without tension to achieve the desired thickness and then were overwound with a spiral wrapping of 0000 silk thread applied firmly. This wrapping was applied with a 3 mm. gap between the spirals, leaving the bulk of the graft relatively uncompressed (Fig. 1). Within the layers of Ivalon was incorporated a sheet of open-weave Dacron or Fiberglas fabric which encircled the prosthesis with a slight overlap; this resulted in "burying" the reinforcing material within the sponge so that it does not present on either surface. A wall thickness of 6 mm. before compression, which

Fig. 1.—The method of reinforcement of the polyvinyl sponge and construction of an arterial prosthesis. *A* shows the sheet of Ivalon being rolled on a glass rod with the reinforcing net *c* being laid in place. *B* illustrates the position of the reinforcement *c* within the layers. *C* shows the spiral overwinding for spaced compression and *D* the prosthesis removed from the rod and cut for insertion; *b* illustrates the uniform compression at the area of overwinding which was subsequently abandoned in favor of using a site such as *a* for anastomosis.

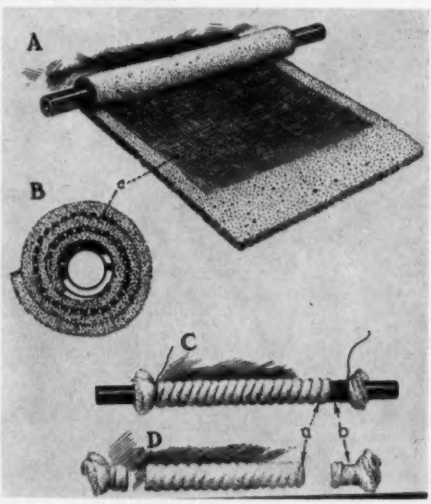

TABLE 1.—*Abdominal Aortic Prostheses*

No.	Diameter, Mm. Aorta/Prosthesis	Material *	Days Followed	Patency	Comment †
Oversized					
1	4/6	I	30	+	
2	4/7	I-G	1	—	Thrombosis
3	4/6	I-G	192	—	Thrombosis
4	4/7	I	54	—	Thrombosis
5	5/8.5	I-G	1	+	
6	5/6	I-D	1	—	Thrombosis
7	5/7	I-G	81	+	Rupture DSL
8	6/11	I-G	432	+	
9	6/11	I-G	196	—	Thrombosis
10	6/8.5	I-G	424	+	
11	6/8	I-D	370	+	
12	6/7	I-D	75	—	Thrombosis
13	6/7	I	87	+	
14	6/7	I-G	4	—	Thrombosis-Hematoma
15	6/7	I-G	200	+	
16	7/11	I-G	4	+	
17	7/11	I-G	27	+	
18	7/8	I-G	18	+	
19	7/10	I-G	4	+	
20	7/8	I-D	75	+	
21	7/9	I-G	424	+	
22	8/11	I-G	28	+	
23	8/8.5	I-G	457	+	
24	8/11	I-G	83	—	Thrombosis-Hematoma
Equal					
25	4/4	I-G	1	—	Thrombosis
26	6/6	I	1	—	Thrombosis
27	8/8	I-D	67	+	
28	9/9	I	155	+	Aneurysm
Undersized					
29	7/6	I-D	149	+	
30	8/6	I	166	+	
31	8/7	I-D	13	+	
32	8/7	I-G	180	+	
33	8/7	I-D	361	+	Stenosis SL
34	8/7	I-G	179	+	
35	8/5	I-D	1	—	Thrombosis
36	8/7	I-G	33	+	Rupture DSL
37	8/7	I-D	100	+	
38	9/7.5	I-D	28	+	Rupture DSL
39	9/7	I	182	+	Stenosis

* I=Ivalon; I-G=Ivalon reinforced with Fiberglas net; I-D=Ivalon reinforced with Dacron net.
† SL=Suture Line; D=Distal

reduced to approximately 2.5 mm. (in the "uncompressed" areas) after overwinding, seemed optimum from the standpoint of controlling the bleeding through the wall without unnecessary thickness.

For comparison, a number of prostheses were made without reinforcement.

In the earlier part of this study the point of intended suture on the graft was compressed by multiple turns of winding thread (Fig. 1); after removal from the mandrel, the graft was cut at these compressed areas. Subsequently, it was found that tissue adherence at this compressed area was less secure than over the remainder of the graft, and in the latter part of the study this type of uniform compression was eliminated.

Sterilization by boiling in distilled water for 20 minutes fixed the prosthesis in shape and left the graft somewhat softer than sterilization in the autoclave.

After the wrapping was unwound, the wet graft could easily be slipped off the mandrel. It was now seen to resemble roughly a crimped tube with thin grooves marking the former position of the wrapping on the outside. It had considerable resistance to wrinkling or buckling with moderate curvature.

Grafts were preclotted either with blood or with a solution of fibrinogen followed by a solution of thrombin.

A total of 61 prostheses were placed in mongrel dogs: 39 in the abdominal aorta, 7 in the thoracic aorta, 2 from the thoracic to the abdominal aorta, and 13 in the femoral artery. Abdominal and thoracic grafts ranged from 5.5 to 6.0 cm. long; the two thoracoabdominal prostheses were 33 and

35 cm. long respectively, and the femoral grafts were 2.5 cm. in length.

Prostheses were selected of such size that the luminal diameters in some experiments were larger than the host vessel, in some cases smaller, and in some the diameter of prosthesis and host vessel were matched. Diameter of host vessel was obtained by measuring the outer diameter with calipers before appreciable dissection was done and subtracting the estimated thickness of the vessel wall.

Operating Technique.—Operations were performed under sterile conditions with use of intraperitoneal pentobarbital (Nembutal) anesthesia. Prostheses were placed in the abdominal aorta below the renal arteries, in the upper thoracic aorta, or in the midfemoral artery. A portion of vessel approximately 80% of the length of the graft was excised. Anastomoses were made with 00000 Atraumatic silk, continuous over-and-over sutures being used.

The peritoneal folds were sutured back laterally to give free drainage of any blood which might accumulate.

Results

Abdominal Prostheses.—Over-all results with abdominal aortic prostheses are given in Table 1. The duration of follow-up ranged from 1 to 502 days. Animals were killed at any time thrombosis was suspected clinically or at selected intervals. All results are based either on autopsy findings or on angiograms.

Of a total of 39 prostheses, good results were obtained in 22 cases, fair results (stenosis or luminal plaques) in 2, and poor results (rupture, thrombosis, or aneurysm) in 15.

There were five instances of thrombosis occurring within 24 hours of implantation and six cases in which thrombosis was found at later follow-up examination. In two of the latter cases thrombosis appeared to have been caused by compression of the graft from surrounding hematoma. These occurred early in the series, and subsequently the policy was adopted of suturing back the peritoneal folds to allow better drainage, and closure of the incision was delayed for 10 to 15 minutes to allow complete cessation of "weeping" of blood through the wall; no subsequent instances of hematoma were noted.

In three cases there was a separation at the distal suture line causing death (28, 33, and 81 days after implantation). *In each case this appeared to be caused by the sutures pulling out of the host vessel with failure of surrounding tissue adherence at the compressed area on the graft.* These occurred early in the series, and subsequently, when the policy of compression of the graft at the point of suture was abandoned, no further separations were noted.

In one graft made of nonreinforced Ivalon, a large aneurysm developed, which appeared on the verge of rupture at the time of autopsy 155 days later (Fig. 2).

In three cases the graft was patent but moderate stenosis at the suture line was observed due to mural plaques; these are recorded as fair results.

Thoracic Prostheses.—Seven grafts placed in the upper thoracic aorta are summarized in Table 2. There was no instance of thrombosis. In one case leakage at the distal suture line produced a hematoma in the left lung. In three cases there was moderate stenosis at the suture lines, in one case producing a marked dilation of the arch of the aorta. The remaining three cases were patent and considered as good results.

Fig. 2.—A large aneurysm found 155 days after implantation in a nonreinforced prosthesis.

TABLE 2.—*Thoracic Aortic Prostheses*

No.	Diameter, Mm. Aorta/ Prosthesis	Material	Duration Follow-Up	Patency	Comment
40	11/11	I-D	9+	+	Rupture DSL
41	8/ 9	I-D	52	+	Stenosis DSL
42	10/11	I-D	50	+	
43	10/11	I-G	70	+	Plaque DSL
44	10/7	I-D	165	+	Stenosis DSL
45	10.5/11.0	I-G	6+	+	
46	14/11	I-D	111+	+	
		Thoraco-Abdominal			
47	7/9	I-D	502	+	
48	10/11	I-D	13+	+	

Two long grafts (32 and 35 cm. respectively) were placed from the upper thoracic aorta (end-to-end) to lower abdominal aorta (end-to-side). In each the result was good at the time of follow-up.

Femoral Prostheses.—Thirteen femoral prostheses are summarized in Table 3. Two grafts were patent at the time of follow-up (28 and 33 days); 10 grafts were thrombosed, and in one case there was separation at the distal suture line by the same mechanism as previously discussed.

Observations on Technical Factors

Effect of Host-Prosthesis Disproportion. To test the effect of disproportion on functional result the abdominal prostheses were divided into three groups: In one, the diameter of the prosthesis was larger than the host vessel; in the next group the prosthesis was matched in size to the host vessel, and in the other the prosthesis was smaller than the host; these data are included in Table 1. The over-all proportions of good and poor results were not markedly dissimilar; however, the oversized prostheses produced appreciably better results if experiments with small aortas (under 6 mm.) are excluded, since a larger proportion of the "oversized" group had small aortas.

TABLE 3.—*Femoral Arterial Prostheses*

No.	Diameter, Mm. Aorta/ Prosthesis	Material	Duration Follow-Up	Patency	Comment
49 R	3.5/3.6	I-G	104	—	Thrombosis
L	3.5/3.0	I-G	104	—	Thrombosis
50 R	2.5/3.5	I-D	83	—	Thrombosis
L	2.5/4.2	I-D	83	—	Thrombosis
51 R	3.5/4.5	I	97	—	Thrombosis
L	3.5/3.5	I	97	—	Thrombosis
52	3.0/4.0	I-D	33	+	
53 R	4.0/6.0	I-D	28	+	
L	4.0/4.0	I-D	14	—	Rupture DSL
54 R	4.0/3.5	I	2	—	Thrombosis
L	4.0/4.2	I	2	—	Thrombosis
55 R	4.0/4.0	I	178	—	Thrombosis
L	4.0/6.0	I	178	—	Thrombosis

Effect of Diameter.—In the experiments with aortic diameters over 6 mm., 17 of 21 prostheses had either a good or fair result. The four poor results were due to aneurysm (1), rupture (2), and hematoma with compression (1). There was no instance of primary thrombosis in this group.

In the group 6 mm. in diameter or less, only 7 of 18 obtained good or fair results and there were 10 instances of thrombosis.

Effect of Material.—The materials used in various grafts were subdivided for analysis into those composed of Ivalon alone, those of Ivalon reinforced with Fiberglas fabric, and those of Ivalon reinforced with Dacron net. No marked difference was noted between these groups. The only instance of aneurysm occurred in a prosthesis made of nonreinforced Ivalon.

Changes After Implantation.—In the first few hours after placement, a pink fibrinous lining developed in the lumen approximately 0.5-1.0 mm. thick. This quickly rounded off the shoulder created at the line of anastomosis, tending to be slightly thicker at these areas. During the subsequent several weeks this layer became paler and was progressively replaced by an opaque white densely adherent lining growing in from either end (Fig. 3). Scattered punctate, hemorrhagic-appearing areas were frequently present during this period, and occasionally small bare ulcerations were seen. This lining could be separated rather easily during the first few weeks but thereafter became tightly adherent. The surrounding tissues quickly became adherent to the grafts and after one or two weeks could be separated only with difficulty. The exception was in those cases with compression at the suture lines as noted previously. The absence of surrounding reaction was quite

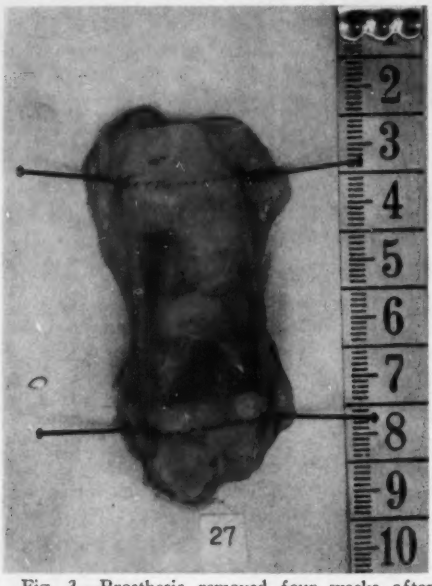

Fig. 3.—Prosthesis removed four weeks after implantation. A smooth, white, intimately adherent neointima is growing in from either end to replace the original fibrinous lining.

remarkable, and the tissue seemed to fuse with the grafts without the surrounding capsule of fibrous tissue so frequently seen with prostheses.

Comment

Others have noted the desirable characteristics of polyvinyl sponge for fashioning vascular prostheses, but enthusiasm has been tempered by subsequent reports of aneurysm formation and rupture due to the lack of inherent strength.[2,4] To fashion prostheses of sufficient strength with use of Ivalon alone would necessitate prohibitive thickness of the wall and marked compression, with loss of desirable porosity. However, our experience suggests that reinforcement will correct this weakness while retaining all the desirable features of the sponge. The combination of plastics appeared to have no harmful effect. This method of incorporating a reinforcing material within the sponge may be of value elsewhere; for example, in replacing diaphragm or wall of the ventricle as in hypoplasia of the right ventricular outflow tract. In these studies, Fiberglas and Dacron net were used for reinforcement; the general properties of Dacron suggest that it may be the most satisfactory material presently available. The open weave which can and should be used does not interfere with the porosity of the Ivalon. For this purpose a locked weave, available in newer fabrics, is desirable to avoid fraying out at cut edges and to increase strength at the suture lines. The method of construction used, with spaced compression, allows the Ivalon to remain considerably more porous than is the case with the usual type of uniform compression; in addition, "glazing" of the surface does not occur. In the uncompressed state the thickness of Ivalon used was approximately 6 mm.; after removal of the spiral thread, very thin grooves of compression were left, with the "uncompressed" areas reduced to approximately 2.5 mm. in thickness. This thickness of wall appeared satisfactory as a compromise to achieve minimum thickness without excessive leakage of blood.

Our experience indicated that porosity is a most important factor in the use of prostheses. There was a clear relation between degree of tissue adherence and graft porosity as indicated by the markedly lessened adherence at the uniformly compressed ends of the earlier grafts, leading in three cases to suture line disruption. With woven fabrics the porosity must be minimal to avoid excessive bleeding through the wall; as a result the ingrowth of surrounding tissues is hampered and incorporation of the prosthesis does not readily occur. This finding has been well documented by Knox and Bigg.[5] Use of thicker but more loosely woven fabrics of other material might also increase porosity while avoiding excessive bleeding by providing a thicker area for interstitial clotting.

To date, experience with prostheses has indicated that size (diameter) is a limiting factor in thrombosis, approximately 6 mm. appearing to be the minimum size for consistently good results and success being rather uniform with diameters over 8

mm.[4,6,8] This appeared to be the case also with this material, and in grafts over 6 mm. there was no instance of primary thrombosis. As might be expected from this observation, poor results were obtained in femoral prostheses.

The usual reason for avoiding the use of prostheses of greater diameter than the host vessel is that flow speed is decreased and turbulence increased in this area, thereby producing a greater likelihood of thrombosis. The increase in lateral pressure resulting from diminished speed of flow might also predispose to aneurysm or rupture. From this line of thought it has been suggested that undersized prostheses would be more desirable than oversized since these factors would be reversed.[3] Our observations do not well substantiate these theoretical considerations. The incidence of thrombosis and rupture was not appreciably different regardless of relation of host vessel to prosthetic diameter. It would appear, however, that results are poorer with undersized grafts when used in vessels of comparable size to those in the matched and "oversized" groups. The estimation of host size in this study was based on conditions as near normal as feasible, with only the overlying peritoneum divided and no actual manipulation of the vessel. As dissection proceeds, there is a decrease in diameter due to spasm, and after division preparatory to anastomosis there is further shrinkage. The further these manipulations proceed before selection of size is made, the greater may be the error in estimation.

On the whole this material seemed not to be promising as a vascular replacement. The incidence of good results in the abdominal and thoracic aorta was only 63%, and, although this figure could undoubtedly be improved by care in selection of animals, it does not seem to warrant further clinical trial. However, this type of reinforcement may have value for use elsewhere.

Summary and Conclusions

A simple method of reinforcing Ivalon for use as a prosthetic material is described. Ivalon does not appear to be a satisfactory material as a vascular replacement.

Experiments with this material as arterial replacements are presented. The incidence of good results in the abdominal and thoracic aorta was only 63%. However, the development of aneurysm was prevented by reinforcement.

Degree of porosity appeared to be an important factor in tissue adherence and prevention of suture line disruption.

Diameter of host vessel appeared to be a critical factor; success rate was markedly higher when the luminal diameter of the host vessel was over 6 mm.

Disproportion between host vessel and prosthesis does not appear to be a critical factor in functional results; however, it is suggested that the diameter of the prosthesis be at least equal to, or slightly larger than, the diameter of the host vessel.

462 Grider St. (15).

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Balanced Operations for Esophagitis Associated with Hiatal Hernia en Masse

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In a previous communication [1] we described balanced operations in the treatment of persistent esophagitis associated with esophageal hiatal hernia. We also referred to previous discussions [2,3] concerning the classification of associated lesions with hiatal hernia and to theories concerning its probable pathogenesis. We defined esophageal hiatus hernia of the so-called sliding or short esophageal type as a cephalad displacement of the cardia above the diaphragm and called attention to associated infradiaphragmatic lesions. Hiatal hernia en masse is also a malfunction of several of the derivatives of the foregut; the parts of the alimentary canal nourished mainly by blood from the celiac axis and concerned principally with digestion. Thus, in a significant number of patients with hiatal hernia en masse there

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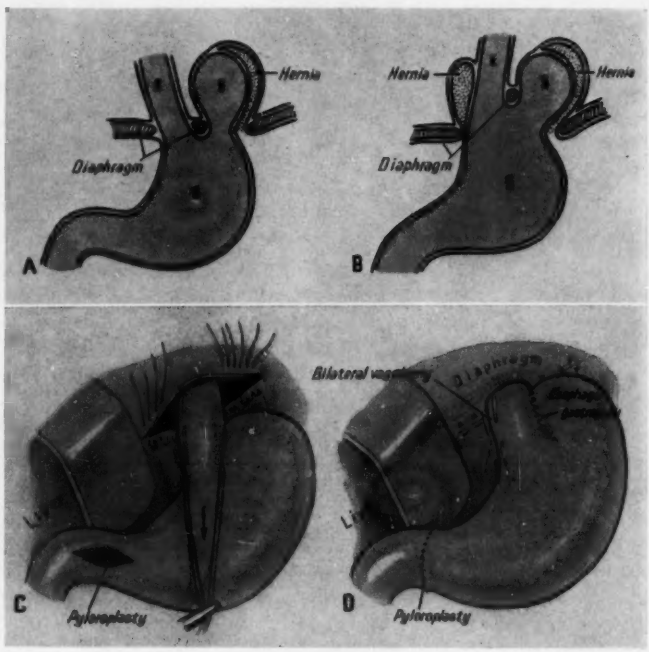

Fig. 1.—*A*, diagram illustrating relations of the esophagus, diaphragm, and fundus in parahiatal hernia. *E*: esophagus. Upper *S*: fundus. Lower *S*: stomach. *B*, diagram of hiatal hernia en masse (combined hiatal and parahiatal hernia). *E*: esophagus. Upper *S*: fundus. Lower *S*: body of stomach. Note that the diaphragmatic fibers and phrenoesophageal fascia in the esophagofundic angle have become attenuated, permitting cephalad displacement of the cardia. The normal cardioesophageal angle (angle of His) is lost. *C*, diagram of balanced operation for esophagitis in hiatal hernia en masse. The peritoneum and phrenoesophageal fascia have been incised and a ½ in. Penrose drain has been placed around the esophagus. The vagi have been divided, permitting more caudal mobilization of the esophagus. The right crus is approximated posteromedially by over-and-over, or mattress, sutures of silk. If the defect is large, sutures may be used anteriolaterally as illustrated in the diagram. Esophagogastropexy is done next, and then pyloroplasty. *D*, diagram of the completed balanced operation in a patient with a large hiatal hernia en masse. The phrenoesophageal fascia is not shown in this diagram. However its posteromedial portion is used to cover the sutured right crus. This adds stability to the suture line and prevents sagging of the esophagus.

is an associated esophagitis, duodenal or gastric ulcer, biliary tract disease, and pancreatitis.

Paraesophageal, parahiatal, or rolling type of hernia is defined as a hernia through the diaphragm in which the cardiac end of the stomach remains below the diaphragm and does so because of the persistence of normal phrenoesophageal fascia or the interposition of some diaphragmatic muscle fibers in the esophagofundic angle (Fig. 1, *A*). The fundus herniates anterior or posterior to the esophagus. Therefore this relatively uncommon type of hernia is in fact not a paraesophageal but a parahiatal hernia and does not often give rise to reflux esophagitis. The angle at which the esophagus enters the stomach (angle of His) (plica cardiaca) is acute and is made so in part by the phrenoesophageal fascia or some muscle fibers of the diaphragm.

Fig. 2.—Lateral x-ray photograph of a 67-year-old man with persistent esophagitis and severe hemorrhage, showing parahiatal hernia which has become hiatal hernia en masse. The cardioesophageal angle is preserved, but almost the entire stomach has moved upward above the diaphragm, "insufficiency type."

Hiatal hernia en masse is a combination of hiatal hernia and parahiatal hernia (Fig. 1, *B*). It probably begins as a parahiatal hernia (Figs. 2 and 3, *A*, *B*), but the phrenoesophageal fascia is deficient. If intervening diaphragmatic fibers in the esophagofundic angle are present, they become atrophic. The hernia then becomes in fact a large type of esophageal hiatus hernia as previously described, and the normal esophagogastric angle may be lost (Figs. 4 and 5). Esophagitis in such instances is a commoner complication. This type is seen more commonly in persons of the lateral type or more obese habitus, and the patients are older than those with so-called sliding hiatal hernia.

Diagnosis and Progress of the Disease

Esophageal hiatal hernia en masse may be asymptomatic. However, many of these patients have an associated esophagitis with annoying symptoms which are more or less typical. They complain of postprandial pain and discomfort, substernal burning or heart burn, dysphagia, and pyrosis. Dyspnea is far commoner than is true in sliding hiatal hernia. Anginoid attacks are frequent; there is regurgitation and aspiration with cough, particularly at night. There may be frequent bouts of vomiting or hematemesis, and an associated secondary anemia. All of the patients reported in this study have had a long period of medical management without benefit. Many have had gallbladder or other operative procedures in an effort to relieve symptoms.

We have recently reviewed the records of 190 patients with all types of hiatal hernia, in which symptoms were severe enough to warrant hospitalization. Definitive surgery was needed by 40 (21%); 17 of these were of the sliding variety and have been reported previously.[1] Our criteria for operations were as follows: (*a*) persistence and progression of symptoms in spite of adequate medical management; (*b*) complications such as stenosis, bleeding or perforation; (*c*) associated lesions for which

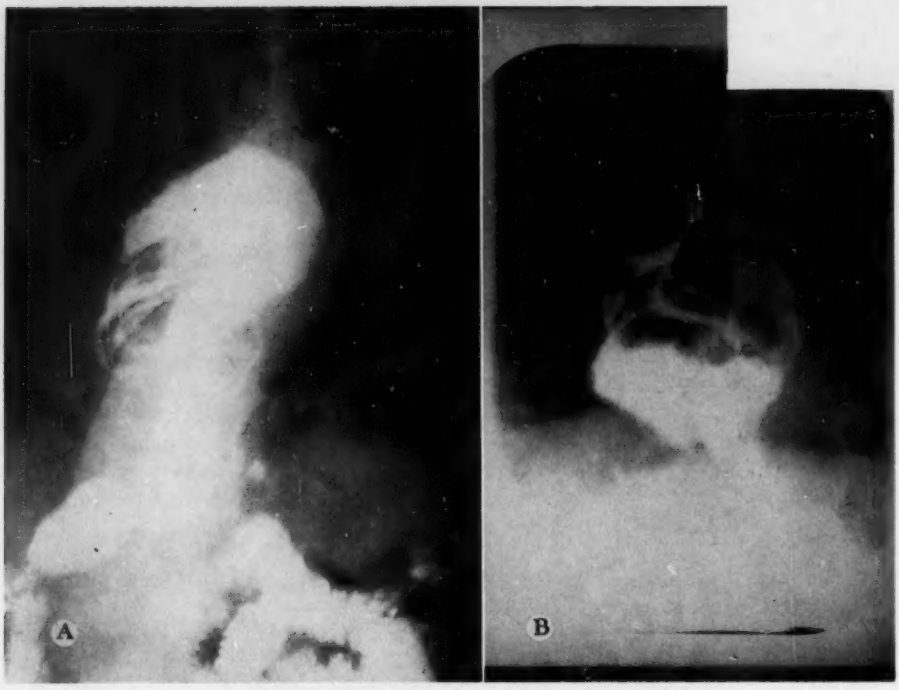

Fig. 3.—*A*, anteroposterior x-ray photograph showing what appears to be a parahiatal hernia in a 59-year-old obese woman with esophagitis. *B*, right anterior oblique view showing same patient nine months later. The normal-appearing esophagofundic angle, as well as a large portion of the stomach, is above the diaphragm.

Fig. 4.—Anteroposterior x-ray showing esophageal hiatal hernia en masse in a woman with esophagitis and duodenitis. The esophagofundic angle is lost, "inverted funnel type."

Fig. 5.—Anteroposterior x-ray showing "inverted funnel type" hiatal hernia en masse. The stomach occupies a more medial position. Frequent anginoid attacks are common in this type.

surgery is indicated, particularly in the gallbladder, bile ducts, stomach, and pancreas.

Treatment

We tried various individual procedures, advocated by different authorities, previously listed,[1] in an attempt to relieve our patients. But we did not obtain consistently good results. The history of our first balanced operations performed eight years ago is described in our previous communication.[1] Our present concept is based on the fact that we are dealing with a disease of several derivatives of the foregut, and that a combination of operative procedures is necessary to obtain complete relief from the harassing symptoms of esophagitis. These operations are done in one stage and consist of the following maneuvers:

1. The stomach is restored to its normal position.
2. The hernia is repaired.
3. Bilateral vagotomy is performed.
4. A normal cardioesophageal angle is obtained by esophagogastropexy.
5. The outlet of the stomach is enlarged by pyloroplasty.

We call the operation "balanced" because it replaces the stomach into the abdomen, reestablishes a normal hiatus and a normal esophagogastric angle, reduces gastric acidity and intragastric pressure, and facilitates gastric emptying. The technique of these procedures differs slightly in some cases from that of balanced operations for sliding hiatal hernia.

A long right paramedian or midline abdominal incision is made, depending upon the patient's habitus and associated disease. It is carried up to the chondrosternal junction, and the sternum may be split to the left of the xyphoid or with a midline incision the xyphoid may be removed to obtain satisfactory exposure. General exploration is then carried out to determine the presence of associated disease. The left triangular (left lateral) and falciform ligaments are cut so that the liver may be depressed and the left lobe retracted well to the right. The phrenoesophageal portion of the transversalis fascia is divided around the esophagus, and the hernia is reduced. Next, the vagi are divided between clamps and tied, thereby permitting greater esophageal mobilization. The esophagus is then pulled downward to the left and anteriorly so that the fibers of the right crus may be approximated medial and posterior to the esophagus. Then the esophagus is moved toward the right and the diaphragm is repaired anterolaterally (Fig. 1, *C*). This step is not always necessary. If the defect is not too large, repair of the right crus as described previously [1] may be sufficient. Esophagogastropexy is carried up far enough to restore the normal cardioesophageal angle. Then the posteromedial portion of the phrenoesophageal fascia is used to cover the suture line and buttress the esophagus so that it stays in position and does not sag. Moreover, the esophagogastropexy by increasing the esophagogastric mass, together with diaphragmatic repair, tends to prevent recurrence, and we have had none in our series. Next the anterior third of the pyloric sphincter is excised and the pylorus is sutured transversely (Fig. 1, *D*). If there are associated lesions of the duodenum, biliary tract, or the pancreas, they are corrected.

Statistical Survey

We have performed one-stage balanced operations for persistent esophagitis associated with hiatal hernia en masse in 23 consecutive cases during the past eight years. Of these, 19 are included in this survey. The ages of the patients varied from 38 to 67 years, the average 56 years. This average is four years older than the group previously described.[1] Twelve (63%) were female and seven (27%) were male. All patients had been on medical management from 5 to 13 years; the average was 6 years as against 4½ years for the previous group. Two (10%) had repeated esophageal dilatations prior to surgery but have required none postoperatively. One had an epiphrenic diverticulum removed by a transthoracic operation, then developed severe esophagitis a year later. Many had unrelated operations before the correct diag-

Fig. 6.—Right lateral x-ray of a 59-year-old man with hiatal hernia en masse, esophagitis, and gastric ulcer with crater (arrow). The esophagus enters the cardia at a right angle.

nosis was established. Four patients had cholecystectomies before we were asked to see them, and four others had cholecystectomy at the time of the balanced operations by us, an incidence of gallstones in hiatal hernia en masse of 42%. Two patients (10%) had diverticulosis with gallstones (Saint's triad).[2,3] Two patients had associated duodenal ulcers, one a gastric ulcer (Fig. 6), and one a postgastrectomy marginal ulcer. In each instance there had been repeated hemorrhage, for which gastrectomy and the balanced operations were done. These four cases are not included in our percentage calculations because gastrectomy alone has been used in the treatment of esophagitis. This might lead to the justifiable conjecture that the gastrectomy rather than the balanced operations produced the good results which were obtained in every case. There was no mortality from the operations, and all patients have been completely relieved of their symptoms for periods varying from one to eight years: average, three years and two months.

Summary and Conclusions

Esophageal hiatal hernia en masse with associated esophagitis is a serious and persistent disease and is more likely to be present in obese, slightly older persons than is hiatal hernia as previously described.

We believe that the disease is an expression of malfunction of several derivatives of the foregut.

In attempting to remedy this malfunction we have used "balanced" operations, consisting of (*a*) restoration of the normal position of the esophagus and stomach; (*b*) bilateral vagotomy to reduce hyperacidity, which is usually present; (*c*) esophagogastropexy to restore a normal esophagogastric angle; (*d*) pyloroplasty to permit ready egress of gastric contents through a widely open pylorus and thereby reduce intragastric pressure; (*e*) correction of any associated disease.

With this procedure we have obtained uniformly good results in a series of 19 consecutive cases, which have been followed from one to eight years.

23 E. Ohio St. (4).

Addendum

The resected anterior portion of the pylorus showed changes which the pathologists described as gastrititis, duodenitis or both in varying degrees in 24 (38.7%) of the 62 cases of all types of esophageal hiatal hernia operated upon to date.

Two additional patients with epiphrenic diverticulum of the esophagus and hiatal hernia have been treated with balanced procedures. Early results are excellent.

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Experiences with Vascular Abnormalities About the Parotid Gland and Upper Neck

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Aneurysms and arteriovenous fistulae in the region of the parotid gland, pterygoid fossa, and upper neck are rarely seen. This report deals with seven patients in whom such lesions occurred, and whom it has been our privilege to handle during the past four years. In addition to the ablation of a vascular abnormality, the location of the lesion imposes an added problem of striving to preserve, if possible, the cranial nerves which are often so intimately involved with the aneurysm. In those cases involving the common or internal carotid arteries, the question of cerebral ischemia also arises when it becomes necessary to ligate these vessels. Thus we are faced with both vascular and neurologic considerations in such patients.

Much of the work of many us in this Society is concerned with the eradication of malignant disease, and in this work the surgical philosophy must be that we stay as far away from the neoplasm as possible, and still retain function to the best of our ability. In contrast to this attitude, the problem under discussion is non-neoplastic, and a different philosophy must be applied. We should stay as close to the lesion as is practical, and by tedious and often quite prolonged dissection, make every effort to preserve adjacent structures. In this small anatomical area there is a superabundance of both arteries and nerves, many of which are well worth preserving. Before such an erudite audience I shall not enumerate them for fear of an error of omission.

In regard to the intracranial effects of the interruption of either common or internal carotid blood flow, the literature, both general surgical and especially neurosurgical, is replete. I shall not now dwell on this most important and often dramatic phase of the problem, but refer you to excellent and relatively recent reports by Moore and Baker,[12] Thompson and Austin,[23] Fager and Poppin,[6] and De Bakey and Crawford,[3] or older experiences of that pioneer of vascular surgery, Rudolph Matas.[10,11] Worth mentioning, as is so strongly emphasized by Moore and Baker,[12] is the importance of maintaining both normal blood volume and blood pressure in those instances in which carotid blood flow must be interrupted, if one would insure the least likelihood of the development of cerebral ischemia.

In regard to peripheral nerve damage, resulting from the lesion itself, or following surgical intervention, there is very little comment in the literature. Halsted,[9] in 1911, operated on a young girl with a congenital arteriovenous fistula between the external carotid artery and a large adjacent mass of veins in close proximity to the parotid gland. His illustrations demonstrate that he elevated the parotid gland and in its upper portion ligated the superficial temporal vein, but there is no mention of his dissecting out the facial nerve, or of any injury to it resulting from surgery. Reid,[15] in 1925, reported a large arteriovenous fistula between the external carotid artery and the external jugular vein, presenting just below the ear and existing for

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32 years. This was the result of a puncture wound from the point of a scissors at 2 years of age. This was excised successfully, and no mention is made of facial nerve damage either pre- or postoperative. Sampsel and Holcomb,[17] in 1957, reported a false aneurysm of the facial artery which was 1 cm. lateral to the corner of the mouth of a 6-year-old boy. Petitti and Jennings,[18] in 1952, also reported a false aneurysm of the facial artery occurring as a walnut-size mass near the corner of the mouth subsequent to a shell fragment wound in the Korean war. In their review of the literature they stated that they were able to find only two other cases reported of aneurysms about the face, and one of these resulted from the insertion of a Roger-Anderson pin in the mandible. These authors mentioned the desirability of avoiding operative injury to the branches of the seventh nerve, but, considering the sizes and the locations of the lesions in their cases, this posed no great problem. Donald Shedd,[20] of Yale, in a personal communication, has informed me of his experiences with a large cirsoid arteriovenous aneurysm involving the entire thickness of the left cheek. Treatment was begun in 1943, and after the unsuccessful use of both irradiation and the injection of sclerosing solutions, the lesion was attacked surgically in 1954. The operation was carried out in two stages with a total operating time of 13 hours. The facial nerve was preserved, and the final result has been excellent.

One of our cases presented a congenital arteriovenous fistula which arose in the pterygoid fossa. We were able to find in the literature only three case reports of similar conditions in this location which presented somewhat the same difficult problems of exposure and extirpation.

Our seven cases can be roughly divided into two groups. In the first group there are four cases in which the arterial or venous abnormality is primarily in the face. In the second group there are three cases in which the lesion is in the upper neck. Of the seven cases, there are four which are either spontaneous or congenital, two which are traumatic in origin, and one which is a false aneurysm occurring one month after a neck dissection for malignant disease.

Diagnosis in many instances is not difficult. There is usually a pulsating mass which is expansile in character, and which is associated with a palpable thrill and an audible bruit. With an aneurysm the thrill and bruit will be systolic in nature, whereas with an arteriovenous communication, the thrill and bruit will be continuous but with a systolic accentuation. A history of trauma, usually a stab or gunshot wound, is frequently elicited with the latter type. However, exact diagnosis is not always so simple. In one instance of internal carotid aneurysm in a 6-year-old girl, we disregarded the previous operative findings of another surgeon. He had evacuated a large quantity of old blood clot from a tonsillar mass, and at our operation four months later it was not until we exposed a pulsating mass in the upper neck that the true pathologic condition became apparent. In another case the vascular abnormality was primarily venous, and the exact nature of the disorder was not appreciated until the venous pressure in the area was increased, either by the Valsalva maneuver or by having the patient place her head in a dependent position.

I missed the correct diagnosis of a false aneurysm of the carotid bifurcation in a soldier in Italy in 1944. He had suffered a bullet wound of the cheek and neck, and it was the rupture of the aneurysm with massive hemorrhage from the pharynx which forcibly called my attention to the true nature of the condition. Fortunately ligation of the common, internal, and external carotid arteries resulted in no untoward sequelae. In contradistinction to the previously mentioned failure to appreciate the presence of an aneurysm, it is also possible to erroneously diagnose the presence of one. After the preparation of this report was begun, a 65-year-old white

woman presented herself with a pulsating mass just below the angle of the mandible. This mass was also displacing the left tonsil toward the midline. All observers felt certain that this pulsation was expansile and that we were dealing with an aneurysm of the internal carotid artery. With the patient under local anesthesia, I occluded the internal carotid artery with a Potts clamp for 30 minutes to determine if the patient could tolerate its obliteration. Since there was no neurologic deficit resulting from this maneuver, the patient was put to sleep; the incision was enlarged, and the true diagnosis was ascertained. We found not an aneurysm but a large carotid body tumor arising from the upper end of the vagus nerve, beneath the internal carotid artery. The pulsation had been a transmitted one and was not expansile in nature.

Apropos of carotid body tumors, and our discussion of cranial nerve damage subsequent to surgery in this area, Sessions and others,[18] at Vanderbilt University Hospital recently analyzed some 15 such cases which have been treated there since 1925. They commented on the fact that 10 of the 15 cases operated upon suffered some degree of cranial nerve or cervical sympathetic nerve injury at operation. Their observations further emphasize the difficulty of preventing surgical injury to cranial nerves when working in this locale.

The first case report concerns a large congenital arteriovenous fistula arising in the pterygoid fossa and presenting in the cheek and upper neck. This was our first aneurysm in which there was intimate involvement of the facial nerve, and in this instance we were unable to preserve the nerve. The reasons for this failure will be evident, but having now had further experience with three additional related lesions in this general location, I would try harder to preserve the seventh nerve should I again have a similar problem.

CASE 1.—This 22-year-old white woman was seen in consultation on March 3, 1956, on the neurosurgical service of Dr. William Meacham. She had been admitted with a 10×10 cm. soft boggy mass of the left cheek and upper neck. X-ray of the skull revealed a punched-out area of decreased density in the left parietal area. A carotid arteriogram revealed a normal internal carotid artery, and no "feeding vessel" to the site of the skull defect. On examination we found the patient to have the above-mentioned mass extending from the tragus forward to the corner of the mouth and nasal ala, and down over the angle of the mandible onto the upper neck and back to the mastoid. There was an expansile pulsation in the mass, and a continuous "venous hum." In the left floor of the mouth there was a firm 2×2 cm. nodule, many dilated veins, and some slight fullness of the left tonsillar area. The temporal and angular veins were markedly dilated. Three transverse scars were present on the left neck and cheek. The past history explained these scars, for the patient had had three previous operations for this condition. The first operation was done in Birmingham in 1953, with a diagnosis of "angioma of the left external carotid artery," and the operation was stated to have been "ligation and excision of an aneurysm." The second operation was done in Florence, Ala., in 1954 with a diagnosis of an aneurysm of the left superficial temporal artery, and the external carotid artery was said to have been ligated. The third operation was done in St. Louis by a member of this Society. His operation was of necessity limited because the family of the patient insisted that nothing be done to jeopardize her facial nerve. In a letter to me, this surgeon stated that he dissected out the facial nerve and the mass as far as possible, and found that the patient had an aneurysm extending from the upper neck into the substance of the parotid gland, up beneath the zygoma and posterior to the ramus of the mandible toward the base of the skull. Fibers of the seventh nerve coursed over the pulsating lesion. The mass was aspirated with a small needle, and bright arterial blood was obtained. Further dissection was impossible without seventh nerve destruction. The above-mentioned surgeon suggested to me that the radical removal of this aneurysm, if at all possible, would certainly require sacrifice of the seventh nerve and some of the ramus of the mandible. He voiced doubts as to the ability of controlling bleeding at the base of the skull.

With this history and good advice, and with the full consent of the patient and her family to sacrifice any structures necessary, including the seventh nerve and mandible, I operated on this young woman on March 26, 1956. No attempt was made to preserve the facial nerve, and the mandible was divided through the sigmoid notch. The coronoid and condyle were removed. The mass extended posterior to the upper end of the mandible, where numerous large veins entering the

mass were divided. Near the base of the styloid process the sac narrowed to a diameter of 1.5 cm., and entering the sac here I found a large artery and accompanying vein. These were separately ligated and transfixed, and the aneurysmal mass, obviously now an arteriovenous fistula, was excised. I am unable to identify positively the artery, though it might well have been the internal maxillary. The dissection was quite bloody, and six pints of blood were required for replacement. There has been no recurrence of the aneurysm in the three years since operation. The mass in the floor of the mouth has disappeared. The left temporal and angular veins have remained prominent. Proptosis and chemosis of the opposite eye have developed, with paralysis of the right external rectus muscle. Numerous sebaceous and warty excrescences of the skin of the face have persisted. Headaches were prominent for several months postoperatively, but have now subsided. On June 20, 1958, Dr. Greer Rickettson inserted fascial slings which have helped to overcome facial disfigurement.

At present the patient is attending college, and appears to be well accommodated to her less than attractive appearance. Her dental occlusion is normal.

Comment: The difficulties inherent in such a case are obvious. Exposure is one of the major problems. We were compelled to divide the mandible to provide access to the bulk of the aneurysm, and even with the sacrifice of the facial nerve and of the mandible above the sigmoid notch, there was no assurance that we would be able to control bleeding in the pterygoid fossa and at the base of the skull. Fortunately this was safely accomplished.

Permanent cure of such fistulae may be difficult. The previously mentioned case of Halsted was reoperated upon in 1918 by Reid, at which time a recurrence was present because a small communicating artery had been left at the original operation. After this second operation a slight bruit persisted, and when the patient was seen four years later, there was a pulsating mass below the lobule of the right ear and there were dilated veins of the face and of the eyelids. Again the typical thrill and bruit of an arteriovenous communication were present, and these could only be obliterated by compression of both common carotid arteries. Elkin [6] has stated that in order to cure permanently an arteriovenous fistula it is necessary either to excise or to ligate the fistulous communication. Barney Brooks [1] in 1931 reported the introduction of a small piece of muscle into an artery to act as an embolus, and thereby to occlude an inaccessible arteriovenous opening. In 1947 Drs. Gerbode and Holman [8] employed this method in the treatment of a congenital fistula located between the right internal maxillary artery and a large vein in the pterygoid plexus. The external jugular vein, which was pulsating, was ligated, as were the branches of the external carotid, and a 5×0.3 cm. strip of muscle was inserted into the external carotid artery. The lower end of the strip of muscle was sutured at the site of its insertion, and its upper portion was allowed to be carried up to the communication by the force of the blood stream. Subsequent to this the carotid was ligated and divided. One month after operation the bruit was absent, but two and a half months after operation a faint bruit could be heard just in front of the ear, and this bruit could only be stopped by pressure obliteration of the opposite carotid artery.

In 1951 Mims Gage [7] reported a similar case in which a venous sac, partially hidden beneath the angle of the mandible, communicated with the external carotid artery, as well as with dilated anterior and posterior facial veins. After division of the artery and veins below the sac, arterial blood could still be seen circulating in the thin-walled sac. Apparently not aware that Gerbode and Holman had previously employed a similar method in their case, Gage packed the sac with 10 small pieces of muscle, introducing these through the cut end of the posterior facial vein. Examination four months after operation revealed no recurrence of the bruit.

In 1955 Casiraghi and Thompson [2] reported from Buenos Aires the case of a 61-year-old woman with an arteriovenous communication between the internal maxillary artery and a vein of the pterygoid plexus. The mass presented beneath the

lobule of the ear and resembled a parotid tumor, except for the presence of a thrill, bruit, and its pulsatile character. The facial nerve was dissected from anterior backward; the parotid gland was elevated, and the aneurysm, which was the size of a walnut, was excised. The authors made no mention of either difficulty with adequate exposure, or of need for resection of the mandible. Facial palsy, which resulted from traction on seventh nerve fibers, disappeared in three months.

We do not believe that any of the abovementioned methods of handling a somewhat similar situation would have been feasible in our case. After our specimen had been removed and opened in the laboratory, the thin-walled sac was found to measure 7×4 cm., and numerous vascular channels entered into it. We doubt that packing this large sac with muscle would have been permanently efficacious.

The next three cases are grouped together because they all primarily involved the cheek. In addition to the vascular lesion, the facial nerve was the prime consideration in each. In all three the vascular abnormalities were within, behind, or adjacent to the parotid gland. In each case, before any attempt was made to approach the lesion itself, the main trunk of the facial nerve was identified, and the dissection was carried anterior in the plane of its ramifications. In this manner, whether the lesion was superficial to, or beneath the fibers, we were able to preserve them. This often required considerable traction and trauma to the nerve, with partial or complete paralysis ensuing postoperatively. However, in each case, function returned in a period of two to six months. There is no question, in our opinion, that the easiest and safest approach to the facial nerve is a direct one to the main trunk before it bifurcates.

CASE 2.—This 19-year-old white youth was admitted to Vanderbilt University Hospital on Oct. 26, 1957. He had been in a car wreck on Oct. 12 and had been admitted to another hospital in an unconscious state, and with temperature of 105 F. It was found that he had basilar skull fractures, fractures of the maxilla and mandible, and a pneumothorax on the right side. He also had cerebrospinal fluid drainage from both ears and from the nose. A pulsating mass in which both a bruit and thrill were evident subsequently developed in the left cheek. The patient was referred to Vanderbilt University Hospital for further diagnosis and treatment. On admission he was found to have marked asymmetry of the face with an 8×8 cm. expansile pulsating mass in the left cheek. A thrill and bruit were present over the mass and both disappeared with compression of the common carotid artery. X-rays revealed fractures of the right symphysis and of the left condyle of the mandible. On Oct. 28, under general anesthesia, an arteriogram of the left common and internal carotid arteries revealed no abnormalities. It was felt that this patient had a false aneurysm of the left external carotid artery with possible involvement of the internal maxillary artery. He was taken to the operating room on Oct. 31, 1957, where a transverse upper neck incision was made with an extension upward in front of the ear. A tape was passed about the external carotid artery just above the posterior belly of the digastric muscle, and the main trunk of the facial nerve was identified. The superficial lobe of the parotid gland was dissected from the facial nerve fibers and removed, and the aneurysm was found beneath the nerve fibers. Both the superficial temporal artery and vein above the mass were divided and a goodly portion of the sac was dissected free before it was inadvertently entered. Bleeding was controlled without excessive difficulty by occluding the external carotid artery proximally, and by digital compression of other feeding arteries. Blood clots were swept out of the sac, and the head of the condyle of the mandible was found lying free within the sac. This bony fragment was removed, along with much of the sac wall, and, though the internal maxillary artery could never definitely be identified as such, it was felt that it probably also was involved. All tributaries were ligated with silk; the neck of the condyle was further shortened with a rongeur, and the wound was closed with silk and drainage. Two pints of blood were given. The postoperative course was smooth. There was moderate weakness of the left facial muscles due to traction on seventh nerve fibers, but this weakness showed progressive improvement. The patient was discharged on his ninth postoperative day, and when he was last seen the facial nerve paralysis had completely disappeared.

CASE 3.—This 17-year-old white youth was admitted to Vanderbilt University Hospital on Dec. 17, 1958 with a five-year history of swelling of his left cheek. This swelling had gradually increased in size, especially in the past year. There was no history of local trauma. The patient had

noted a "throbbing" sensation in the left cheek, but no humming sound had been noticed. Extraction of a left upper molar four years before had resulted in profuse hemorrhage which necessitated hospitalization and the administration of two pints of blood. On examination there was a diffuse, soft 6×8 cm. swelling of the entire left cheek from just lateral to the lip commissure and nasal ala to the tragus of the ear and down to the lower margin of the mandible. The eyelids were not involved. The mass presented a faint, but definite, expansile pulsation over the parotid area, and there was a palpable thrill and continuous audible bruit with a systolic accentuation. The thrill and bruit both disappeared on pressure occlusion of the common carotid artery. X-rays of the facial bones revealed no abnormality. Chest x-ray revealed no cardiac enlargement or pulmonary abnormality. A carotid arteriogram was unsatisfactory.

On Dec. 19, 1958, the patient was taken to the operating room and the cheek and upper neck exposed through a long transverse upper neck incision with an upward prolongation in front of the ear to above the zygomatic arch. This gave adequate exposure as far anterior as the commissure of the lips and the side of the nose. Dissection was begun posteriorly where the main trunk of the facial nerve was identified, and the dissection was carried forward in the plane of the nerve ramifications, elevating the superficial lobe of the parotid gland. The external maxillary artery was found to be some four times its usual diameter, and similarly dilated veins were found in and beneath the parotid gland. The external carotid artery and the posterior facial vein were much larger than are usually seen. Dissection was carried anterior to the lips, upward to the lower eyelid, and behind the anterior margin of the mandible, as well as into the internal pterygoid muscle behind the angle of the mandible. No definite arteriovenous communication could be identified. Therefore the external carotid and facial arteries were ligated and divided, and a considerable segment of each was excised. The anterior and posterior facial veins, as well as other venous tributaries, were excised and the wound closed with drainage. Microscopically, the connective tissue which was removed from the cheek revealed numerous dilated vascular spaces, and the facial vein walls were microscopically somewhat thickened. These findings are compatible with an arteriovenous communication.

Postoperatively the patient has done well. There has been weakness of the left lower lip due to traction on the marginal branch of the seventh nerve, but this is improving. Edema is subsiding. There is no longer a pulsating mass, nor can a thrill or bruit be felt or heard over the cheek.

Case 4.—In August, 1956, this 22-year-old white woman had a sudden onset of swelling in her left parotid region which lasted only six hours. The mass was said to have been the size of a golf ball. Swelling returned the following day, again for six hours, and this was repeated four times. There was considerable associated pain, improved by cold applications, made worse by heat. There were continued intermittent episodes, each lasting longer than the previous one, with the most recent one lasting a week. No redness of the overlying skin was noted. When swelling was present it was difficult for the patient to open her mouth; chewing was painful, and she found it difficult to move her head freely, or to swallow well. There was no history of injury. When first seen she said that at that time there was no swelling in the left cheek and upper neck. Examination in the upright position revealed her face and neck to be symmetrical. However, the Valsalva maneuver produced a 6×6 cm. soft swelling in the left cheek and upper neck. No thrill or bruit were present. Lowering the head below the heart level caused the same mass to appear and it promptly disappeared on raising the head. There was no facial or other cranial nerve weakness. The mass did not pulsate. The pharynx, oral cavity, and eyegrounds were normal. Our impression was that a venous anomaly existed which involved the left parotid area. The patient was admitted to Vanderbilt University Hospital April 15, 1957, and was operated on the following day. A Y-shaped incision in front of and behind the left auricle, and transverse in the upper neck, was made; the main trunk of the facial nerve was identified, and the dissection carried anteriorly, removing the superficial lobe of the parotid gland. We found a

Fig. 1 (Case 1).—Spontaneous arteriovenous fistula in the pterygoid fossa.

Fig. 2 (Case 2).—Traumatic false aneurysm of the external carotid artery, associated with a fracture of the condyle of the mandible.

Fig. 3 (Case 4).—Venous anomaly which lay in and beneath the parotid gland.

Fig. 4 (Case 5).—Traumatic arteriovenous sac and fistula between the upper portion of the common carotid artery and the internal jugular vein. A saccular aneurysm was also present on the posterior wall of the carotid artery.

Fig. 5 (Case 6).—False aneurysm of the common and internal carotid arteries which followed a radical neck dissection.

Fig. 6 (Case 7).—Spontaneous aneurysm of the internal carotid artery arising very high in the cervical portion of the artery.

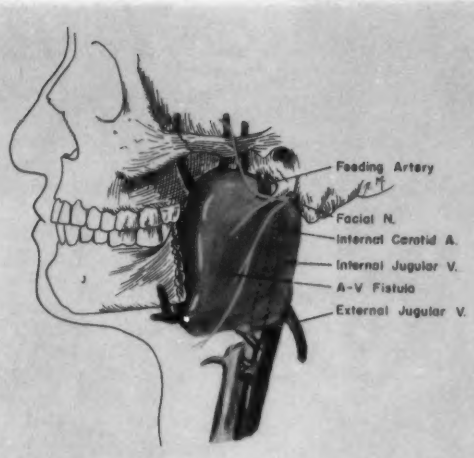

Figure 1

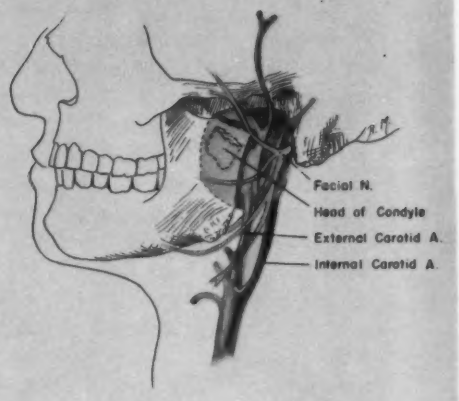

Figure 2

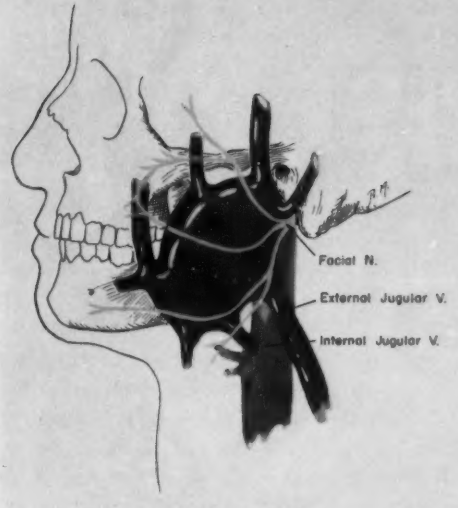

Figure 3

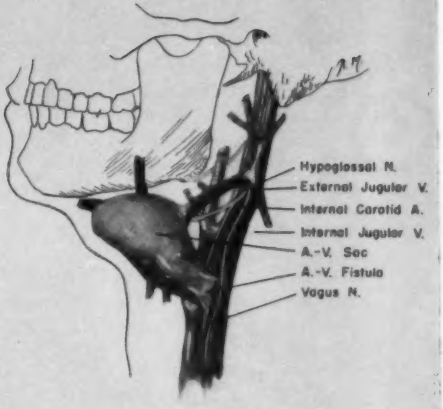

Figure 4

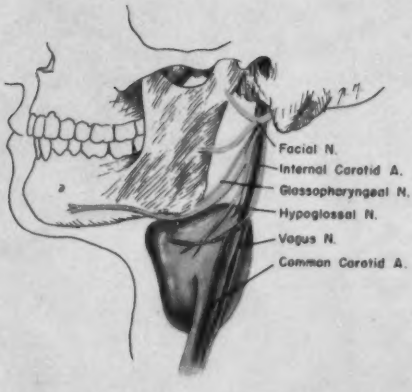

Figure 5

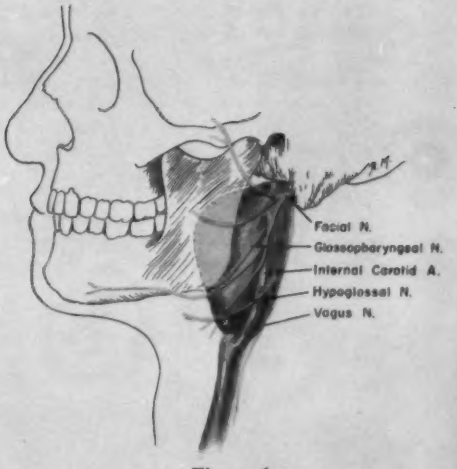

Figure 6

large venous sac beneath the facial nerve fibers with channels extending into the parotid. By elevation of all the nerve fibers with fine silk sutures, the sac was tediously dissected free. It was entered on numerous occasions, and bleeding was profuse. The internal jugular vein was tremendous, as were the posterior facial and external jugular veins. No definite arterial component could be identified. The dissection required four hours, and the patient was given two pints of blood. The wound was closed with drainage. Postoperatively the patient did well, though there was complete facial palsy. Function of the facial muscles began to return in two weeks, and was about 50% of normal in one month, and completely normal in three and a half months. There was no recurrence of the mass when the patient was last seen in December, 1958.

Comment: While Case 4 is not an aneurysm or an arteriovenous fistula, it fits well into this group. Though we were not able to demonstrate either preoperatively or at operation any arterial component, it is possible that this lesion was analogous to an aneurysmal varix, so named by Pratt [14] in describing certain instances of massive and rapidly recurring varicosities of the lower extremities. We have found no report of a similar facial lesion in the literature.

In one of the above cases, we were unable to demonstrate a definite arteriovenous communication. The swelling of the cheek, the pulsatile fullness, the thrill and bruit, the great dilatation of both arteries and veins, and the more than usual thickening of the vein walls, as seen microscopically, all suggested that such a communication, or perhaps multiple small communications, existed.

The final three cases all involved major arteries in the upper neck. In addition to obliteration of the vascular lesion and avoidance of injury to adjacent cranial nerves, there is also in this group the problem of internal carotid blood flow and prevention of cerebral ischemia. All three lesions involved either the common or internal carotid arteries. The single common carotid artery-internal jugular vein fistula is included in this report of upper cervical vascular lesions because the large arteriovenous sac presented just beneath the lower margin of the mandible. An additional common carotid artery-internal jugular vein arteriovenous fistula which occurred low in the neck, and which had existed for some 21 years, is not reported in detail. This case was successfully operated on Sept. 12, 1956, by Dr. William Scott at our institution. In this instance the fistulous tract was divided, and the defects in the artery and vein were closed without interrupting the blood flow in the common carotid artery. This procedure was carried out under hypothermic conditions. There was no injury to the vagus, phrenic, or cervical sympathetic nerves, and at no time was there evidence of cerebral ischemia.

Case 5.—This 41-year-old Negro man was admitted to Vanderbilt University Hospital on Jan. 4, 1959, with a history of having been shot some four months previously with a 38-caliber pistol. The bullet entered just below the mandible and just to the left of the midline, and made its exit in the posterior neck at a somewhat lower level. There was loss of consciousness for approximately one hour, and on regaining consciousness the patient noticed a great amount of blood on his clothes. At this time he also noticed a swelling of the left upper neck, a throbbing sensation, and a "hum." There was also inability to raise the left arm, and there was pain in the left side of the face and the head. Later, on rare occasions, there was slight difficulty in swallowing. Our examination, four months after the injury, revealed a lemon-sized pulsating mass in the left upper anterior neck, over which a strong thrill was palpable, and the thrill was transmitted down the neck to the clavicle. A loud bruit was also present, which was continuous in nature but with a systolic accentuation. Pressure on the common carotid artery below completely obliterated the bruit and thrill and lowered the pulse rate from 76 to 56. The temporal pulse on the left was palpable, but weaker than that on the right. There was no cranial nerve deficit. Blood pressure was 120/70. Preoperative diagnosis was made of an arteriovenous fistula, probably between the external carotid artery and one of the facial veins. The patient was taken to the operating room on Jan. 7, 1959, and a long transverse incision was made from the mastoid, below the mass, to the midline. Later a downward prolongation along the sternomastoid muscle was made. The common carotid

artery was isolated, a tape passed around it, and occlusion of the artery partially collapsed the mass. After considerable tedious dissection, the large sac was dissected free and the anterior and posterior facial veins were found to enter the sac. The mass was dissected backward toward the carotid artery where it narrowed to a 2 cm. neck across which a serrefine clamp could be placed. It was then realized that the neck communicated with the common carotid artery and the internal jugular vein, and not with the external carotid artery. The vagus nerve was found to be adherent in the mass between the common carotid artery and the internal jugular vein. In addition a 1×1 cm. saccular aneurysm was found on the posterior aspect of the common carotid artery. The communication was some 2 cm. below the bifurcation of the common carotid. The internal jugular vein was divided both above and below the fistulous opening, and it was found that by resecting some 2 cm. of the common carotid artery both the saccular aneurysm and the fistulous communication could be removed. Accordingly, with arterial clamps both proximal and distal, this segment was excised, the fistula and aneurysm both removed, and an end-to-end suture of the common carotid artery carried out without difficulty. Interruption of blood flow in the artery was for only 14 minutes. By careful dissection the vagus nerve was preserved. Care was taken to preserve the hypoglossal nerve and the marginal branch of the facial nerve. The patient's postoperative course was most uneventful. A good temporal pulse was present after his return to the recovery room, and, though there was slight hoarseness, this had improved considerably by the time of discharge from the hospital on the sixth postoperative day. There was no evidence of any cranial nerve damage other than this, and there was at no time any evidence of cerebral damage. The pain in the shoulder and face had completely disappeared.

Case 6.—This 36-year-old white man was admitted to Vanderbilt University Hospital on Feb. 28, 1955. Two years previously he had become hoarse, but it was not until August, 1954, some 18 months after the onset, that a biopsy was performed at a hospital in Kentucky, revealing squamous cell carcinoma. The patient was given deep x-ray therapy, but a repeat biopsy several weeks after completion of therapy revealed a persistence of the disease. In January, 1955, he had a total laryngectomy, and at this time carcinoma was found to have perforated through the larynx and to have extended into the ribbon muscles. Also large lymph nodes were noted in the left side of the neck. The patient was referred to us in February, at which time he was found to have a 4×4×3 cm. hard left upper cervical mass. On March 1, a left radical neck dissection was carried out, and though the common and internal carotid artery walls did not seem to be invaded by tumor, there was definite tumor in the carotid sheath, which was excised with the specimen. The vagus nerve and external carotid artery were also excised. Carcinoma had extended into the wall of the internal jugular vein. The postoperative course was uneventful, and the patient was discharged some 10 days later. He reentered Vanderbilt University Hospital in approximately one month, with a one-week history of swelling of the left neck. In the two days prior to his entering the hospital, the mass had more rapidly enlarged, and a correct diagnosis of a false aneurysm of the carotid artery had been made by his family physician. This was confirmed on admission to our hospital at which time a 6×6 cm. pulsating mass was present in the left middle and upper neck. As there was a little bleeding from a site of drainage, the patient was taken to the operating room on the day of his admission. The carotid artery was isolated low in the neck, and a tape was placed about it. As we had the advantage of knowing that the external carotid artery had been sacrificed at the previous operation, there was no difficulty in opening into the sac with proximal control of the common carotid, and the bleeding from the internal carotid artery above was easily controlled with digital pressure. The internal carotid artery was dissected upward and occluded with a Potts clamp and the large aneurysmal sac was excised. Microscopic sections revealed no evidence of tumor in the aneurysmal sac. A freeze-dried arterial homograft was reconstituted but was found to be too small in caliber, and accordingly another was prepared. This fitted quite well and was sutured into the defect, spanning a distance of some 5 to 6 cm. Postoperatively the patient did well for the first 30 hours, and then developed a sudden hemiparesis on the right, with aphasia. His general condition remained good, and he was able to return to his home on April 19, some 16 days after his operation. Over the next few months his aphasia and paresis improved but did not completely disappear. He subsequently developed metastases in the right lower neck and mediastinum, and died on Dec. 6, 1955.

Case 7.—In February, 1958, a mass was noted in the left upper neck of this 6-year-old white girl. In March, under intratracheal anesthesia, that which was thought to be a retropharyngeal abscess was drained by a competent otolaryngologist, and the surgeon commented on the large quantity of old blood clot that was obtained, and the paucity of purulent material. Postoperatively the patient did well. At the time of this first admission, a Horner's syndrome on the left side

was present. The mass in the neck and pharynx persisted, and the patient was referred to me July 29, 1958. We found her to have a 4×2 cm. left posterior pharyngeal and tonsillar mass, without ulceration or pulsation, and in the left upper neck there was a hard deep nodular fixed 3×3 cm. mass beneath the angle of the mandible. The general examination and laboratory work were noncontributory. There was pulsation of the cervical mass, but I was under the impression that this was a transmitted pulsation and I could not feel a thrill or hear a bruit. However, Dr. William Stoney, the resident on the case, felt the pulsation to be expansile, and also thought he could hear a bruit. Because of his astuteness, an aneurysm was one of the preoperative diagnoses entertained. On Aug. 5, a transverse upper neck incision was made, and several large lymph nodes were removed from the anterior surface of the internal jugular vein. These appeared grossly to be normal. Beneath this area and beneath the internal and external carotid arteries there could be felt and seen a bluish mass of considerable size. Palpation revealed the mass to be pulsating, and a thrill was readily evident. The incision was enlarged; the external carotid and superior thyroid arteries were transfixed and divided, and the common and internal carotids were retracted laterally. This exposed a thin-walled blue pulsating mass. Application of a Potts clamp across the internal carotid did not appreciably diminish the tenseness or the size of the sac. By careful dissection some half of this 6×4 cm. mass had been delivered when it was entered. Forceful arterial bleeding flooded the field in spite of occlusion of the internal carotid below. Quickly the sac was widely opened, blood clot swept out, and the bleeding controlled by finger pressure at the neck of the sac, which was high near the base of the skull. This area was oversewn with several silk sutures placed beneath the occluding finger, giving good hemostasis. The internal carotid artery was ligated below. One pint of blood was given. The wound was closed with silk with drainage, and a tracheostomy was performed. During the dissection great care was taken to preserve the vagus nerve, the hypoglossal nerve, and the marginal branch of the seventh nerve. However, ligation of the upper end of the internal carotid artery was necessarily carried out without adequate visualization, and the danger of damage to cranial nerves here was great. The postoperative course was moderately stormy. For several days the child was unable to eat without coughing, and she was therefore fed by means of a polyethylene tube inserted through her nares. The tracheostomy tube was removed on the fourth postoperative day. She was hoarse and had a nasal twang to her voice; her tongue deviated to the left on protrusion; there was paralysis of her left lower lip, and the Horner's syndrome persisted. She was sent home on the 12th postoperative day, taking food adequately by mouth. There has been progressive improvement with disappearance of the hoarseness, of the tongue deviation, and of the lower lip palsy. The neck and pharynx now appear normal, and the only neurological deficit remaining is a slight nasal tone to the voice. The Horner's syndrome has disappeared. The patient eats normally, and has gained weight. At no time was there evidence of cerebral ischemia, which would be anticipated in view of the forceful back bleeding from the upper end of the internal carotid artery.

Comment: In Case 6, the case of the false aneurysm of the common and internal carotid artery following neck dissection, the vagus was of no importance, and had in fact been removed previously. In the absence of the larynx no harmful sequelae follow sacrifice of the vagus nerve. We felt it was worth while to attempt to reestablish common and internal carotid artery blood flow by use of the homograft, since it was impossible to bridge such a large gap by end-to-end suture. We do not know the reason for the delay in the appearance of the paralysis and aphasia, but thrombosis of the graft, with or without propagation of the thrombus upward into the cerebral vessels, is a plausible explanation. Delayed paralysis following internal carotid artery ligation is a hazard well recognized and is mentioned by Moore and Baker [12] as well as by others in their discussions of carotid artery ligation.

In those aneurysms involving the common carotid artery, or involving the lower portion of the internal carotid artery, one might employ the method of De Bakey and Crawford to aid in preventing either immediate or delayed intracranial complications. De Bakey and Crawford temporarily bypassed a large aneurysm of the innominate, subclavian, and proximal carotid by inserting above and below the lesion Lucite cannulae connected by a length of Tygon tubing. Cooley, in the same clinic, used 16-gauge needles connected by tubing as a bypass, but the Lucite cannulae have twice the internal diameter, and, if they are

available, they should be more satisfactory. De Bakey does not feel that one can count on hypothermia in such situations to protect brain tissue from ischemia. He also emphasized the lack of correlation between the duration of carotid occlusion and subsequent evidence of cerebral damage. He cites three cases in which the carotid was occluded for 21, 57, and 65 minutes, after which brain damage ensued, whereas three analogous cases had carotid blood flow interrupted for 19, 67, and 70 minutes without any evidence of harm resulting. There is no doubt that, when feasible, end-to-end suture of the carotid artery, as employed in one of our cases, is preferable. With a little experience this can be done rapidly. The period of occlusion of blood flow in our case was only 14 minutes. Shea and Harrison [19] report an end-to-end anastomosis between the common and internal carotid arteries to bridge a 3.3 cm. defect in which blood flow was interrupted for 65 minutes. Postoperatively there was a left hemiparesis and cloudy sensorium, but both had almost completely disappeared by the 20th postoperative day, and an arteriogram revealed the anastomosis to be patent. The same authors reported another case with a 4.5 cm. defect at the carotid bifurcation bridged by end-to-end anastomosis without untoward postoperative sequelae.

Dimtza,[4] of Zurich, reported an apple-sized aneurysm of the internal carotid artery which was successfully extirpated, with continuity reestablished by end-to-end suture. Cervical sympathectomy was purposefully performed to attempt to improve distal blood flow. Postoperatively there was absence of both palatal and pharyngeal reflexes with difficulty both in swallowing and in speaking. Dimtza attributed these deficits to central nervous system ischemia, but I believe that, in part at least, these deficits may have been caused by trauma to cranial nerves in the neck. Ten months later there was little difficulty in swallowing, and speech was normal. Dimtza emphasized the rarity of aneurysms in the neck, and quoted statistics from two large series in which those aneurysms of the common, external, and internal carotid arteries comprised only 5% of some 530 cases in one series, and only 2.5% of 596 cases in the other series.

Shumacker and Carter [22] in reporting 288 instances of both aneurysms and arteriovenous fistulae in military personnel report five instances involving the internal, three involving the external, and seven involving the common carotid. They emphasize wide exposure made through a properly placed incision to prevent scarring and contracture, and they also emphasize careful attention to the preservation of adjacent nerves, which are frequently imbedded in the wall of the sac. They state that the cervical aneurysms are fraught with the greatest dangers of any in their series. Three of their six major complications and their only two deaths were in patients with lesions in this anatomical location.

Thompson and Austin [23] report excision of a saccular aneurysm which arose from the internal carotid. After the excision the suture line was reinforced with wrapping of fascia lata. They also wrapped four small aneurysms at the bifurcation, using fascia lata, with satisfactory results.

Reid,[16] in 1926, reviewed 12 cases, which had been treated at Johns Hopkins Hospital, of carotid aneurysm in the neck. Ten of these were of the common, and one each of the external and internal carotid arteries. Only four of these were cured by surgery. These were largely treated by either complete or partial proximal ligation. Winslow [24] has shown the greatest interest in cervical internal carotid aneurysm. In 1926 he reviewed the literature in detail, mentioning the first case reported in 1808 by Sir Astley Cooper. Winslow collected 106 cases, of which 70 were operated on. In the group treated surgically there were 46 patients cured; there were 2 improved; there was 1 recurrence, and there were 21 deaths. These were all, in the main, treated by proximal ligation. There were 35 not operated on, with 25 deaths resulting; 6 were unimproved, and 3 were cured. The three cures apparently thrombosed either sponta-

neously, or with the aid of external pressure. Winslow, in association with Shipley,[21] in 1937, again reviewed the literature on this subject and added 18 cases, 2 of which were his and Shipley's. The operation of choice was proximal ligation. There were no spontaneous cures or improvements without operation in this second group. Many of these cases suffered cranial nerve damage, either pre- or postoperative, in spite of the fact that proximal ligation, rather than attempted excision, was practiced. Winslow emphasized the great danger of mistaking a cervical internal carotid aneurysm for a peritonsillar abscess, and stressed that while there may be a large pharyngeal mass, the presence of muscles and a dense cervical fascia may prevent any manifestation of the disease from presenting in the upper neck. Matas,[11] in discussing Winslow's second paper, reported proximal ligation in 18 cases of internal carotid aneurysm. Twelve of these cases were carotid artery-cavernous sinus arteriovenous fistulae with pulsating exopthalmos. There was only one death, a 5.5% mortality. On the other hand, Matas,[10] in 1940, mentioned seven aneurysms of the internal carotid artery in the neck, four of which followed tonsillectomies or tonsillar abscesses. These were treated by total proximal occlusion of the internal carotid artery. There were two deaths, a 28.5% mortality.

It has long been apparent that interruption of internal carotid artery blood flow results in completely unpredictable results. With the excision of an aneurysm of the common carotid artery, we should be able to reestablish continuity in practically all instances by either direct anastomosis or the insertion of either an arterial homograft or a plastic prosthesis. The problem is more difficult when the internal carotid is involved because of a more limited access to the lesion, as well as because of the short length of the vessel between the carotid bifurcation and the base of the skull. Sacrifice of the external carotid artery will often facilitate end-to-end suture. If an adequate length of artery can be obtained above, and if the defect is so great as to obviate end-to-end anastomosis, an arterial substitute should be inserted. A cervical internal carotid aneurysm may be saccular, rather than fusiform, and, if so, it may be excised at its neck, the defect closed, and continuity not interrupted. Perhaps reinforcement of the suture line with fascia lata, if the vessel is sclerotic, might be of added benefit. And lastly, if none of the above-mentioned methods of reestablishing continuity is feasible, then the time-honored principle of proximal ligation, with its often satisfactory but unpredictable outcome, should be employed.

Summary and Conclusions

Seven cases of vascular abnormalities involving the parotid region and upper neck have been presented.

In addition to correction of the vascular lesions, the importance of preserving adjacent cranial nerves is emphasized.

Every attempt should be made to reestablish blood flow in the internal carotid artery before resorting to simple proximal ligation.

The experiences of other surgeons in dealing with similar problems are discussed.

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Emphysematous Necrotizing Pancreatitis

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Acute necrotizing pancreatitis which results in gas formation within the pancreas carries a poor prognosis.

Although the complication of gas production can readily be recognized roentgenologically, relatively few cases have been reported in the literature. Felson,[7] in reviewing the literature, found only seven reported cases [2-4,8-11] and added six of his own. Agnos and Holmes [1] reported five others and found an additional two as reported in case reports from the Massachusetts General Hospital.[5,6] Thus, only 20 cases have been previously reported.

Report of a Case

History.—On Feb. 6, 1956, a 58-year-old white man was admitted to Beth Israel Hospital with a 24-hour history of sudden onset of severe upper abdominal pain, nausea, and vomiting following the ingestion of a meal. The pain was constant, severe in nature, extended across the entire upper abdomen and radiated to the back. He had not noted any chills, fever, jaundice, or dark urine.

There was no antecedent history of any similar episodes. Fifteen years ago he had been told that he had a "stomach ulcer" but he had been asymptomatic since then. There was no history of diabetes.

Physical Examination.—The patient was an obese white man who appeared acutely ill. Blood pressure 200/100; pulse 120; respirations 32; temperature 102.4 F. There was no icterus or cyanosis of skin, sclerae, or mucous membranes. He was markedly dehydrated. The lungs showed fine dry crackling rales at both bases posteriorly. Heart sounds were of good quality and a tachycardia was present with regular sinus rhythm. The abdomen was distended and tense, with marked tenderness and muscle spasm in both upper quadrants. No rebound tenderness was present. There was a questionable mass in the right upper quadrant. The remainder of the examination was essentially negative.

Laboratory Data.—Urinalysis on admission showed albumin 1+, glucose 2+. The hemoglobin was 15.6 gm. %, hematocrit 38 vol. %, WBC 23,450, with a marked left shift. The serum amylase was 508 units, bilirubin 2.55 mg. %, alkaline phosphatase 3.3 units, thymol turibidity 2.7 units, Na 132.3 mEq/liter, CO_2-combining power 49.1 vol. %.

Fig. 1.—Film of the upper abdomen showing moderate distention of the colon, with no abnormal findings in the region of the pancreas.

X-ray examination of the abdomen taken on admission was reported as follows (Fig. 1): "There is some distention of loops of small bowel in the right lower quadrant. There is moderate distention of segments of the colon. No opaque calculi are noted." X-ray examination of the chest showed bilateral pleural effusions.

Course in the Hospital.—A diagnosis of acute pancreatitis was made and the patient treated accordingly with nothing by mouth, continuous nasogastric suction, intravenous fluids, penicillin, streptomycin and tetracycline (Achromycin), propantheline (Pro-Banthine) I. M., and sedation.

Within 48 hours, with fluid and electrolyte replacement, his temperature fell to 100 F; the amylase dropped 111 units; and serum electrolytes were brought within normal range, but his serum calcium was reported at 3.9 mEq/liter.

His abdominal distention continued however, and after a week his temperature climbed to 102-104 F, and remained elevated. He was unable to tolerate oral feedings, and nasogastric suction had to be continued. In the second week a large upper abdominal mass became palpable extending from the right to the left costal margins. This was thought

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Fig. 2.—Film of the upper abdomen showing numerous radiolucent circular shadows in the region of the pancreas. These are definitely not within the gastrointestinal tract.

to represent a huge, swollen, edematous pancreas with retroperitoneal exudate and possible pesudocyst formation.

Approximately 18 days after admission it became apparent that he was developing almost complete upper intestinal obstruction with profuse nasogastric drainage. He required 4,000-5,000 cc. of intravenous fluids daily to keep him adequately hydrated.

Three weeks after admission repeat x-ray examination of the abdomen now showed the following (Fig. 2): "A Levine tube is noted in the stomach. A small amount of gas is noted in segments of the small and large bowel. There is no free air in the peritoneal cavity. Extending from the right upper quadrant across the midline to the left upper quadrant there are numerous unusual appearing radiolucent circular shadows, which are definitely not within the gastrointestinal tract. The appearance suggests a gas-producing suppurative process. The location of the gas bubbles is in the region of the pancreas. Impression: Gas producing suppurative process in the region of the pancreas."

On March 3, 1956, laparotomy was performed, and a huge abscess of the lesser sac was drained through the gastrocolic omentum. The abscess involved the entire pancreas, and large pieces of necrotic pancreatic tissue were removed. Several packings and drains were left in the lesser sac and the wound closed around them with catgut and wire sutures.

Aerobic and anaerobic culture of material from the abscess cavity showed no growth.

The patient improved somewhat postoperatively, but his distention continued and he could not tolerate oral feedings. On the fifth postoperative day a wound dehiscence was noted and was repaired with through-and-through wire sutures. He ran a downhill course, continued to vomit, and became disoriented. On March 14, 1956, 36 days after admission, sudden massive bleeding was noted from the abdominal drains, and despite active blood replacement he rapidly died.

Postmortem examination revealed an almost completely necrotic pancreas with mesenteric fat necrosis and abscess formation. The normal anatomy of the pancreas had been disrupted by the antecedent operative procedure and necrosis. No gross evidence of gas bubbles was seen in this disorganized pancreas. There was erosion of vessels with hemoperitoneum.

Comment

In this case, the gas seen on x-ray was distributed diffusely throughout the pancreas as many tiny bubbles, rather than as a unilocular gas abscess. The gas bubbles were so small and diffuse that they could be confused with colonic or gastric contents. The diagnosis can be made with a reasonable degree of accuracy, if one is aware of the condition. In this case, the radiologist (A. G.), did recognize the gas bubbles as being extraneous to the gastrointestinal tract and in the region of the pancreas.

The pattern of numerous small gas bubbles coincides with the findings in four out of the five cases reported by Agnos and Holmes, in all six of Felson's cases, and in the two case reports from the Massachusetts General Hospital. In contradistinction, all earlier cases reported prior to 1949 were unilocular large gas abscesses of the pancreas. It is possible that the large unilocular abscesses are due to the late coalescence of an earlier diffuse process in patients who managed to survive the acute attack.

There was an interval of three weeks between the first and second abdominal films. While we do not know exactly how long the gas was present, we do know that it definitely was not demonstrable on admission, but developed in the interim. Despite an initial negative abdominal film in acute pancreatitis, valuable information may be obtained by repeated films in patients with progressive symptoms.

Although the gas is probably bacterial in origin, culture from the pus and tissue

removed showed no growth. This may have been due to the massive amounts of antibiotics given prior to surgery or to technical problems associated with the taking of the material for culture.

Of the 21 cases now reported in the literature, 13 are of the diffuse variety and 8 are unilocular gas abscesses. In the eight unilocular gas abscess cases, four are known to have definitely survived and the fate of the other four cannot be determined from the literature. However, the survival rate is at least 50% or better. In contrast, the 13 cases of diffuse emphysematous necrotizing pancreatitis show only 3 (or possibly 4) having survived, with a mortality rate of 70%-77%. This is a much higher mortality rate than that usually associated with acute pancreatitis. Our case also terminated fatally. This adds confirmatory evidence that acute pancreatitis complicated by gas formation has an unusually poor prognosis.

Summary and Conclusions

Acute necrotizing pancreatitis complicated by gas production has an unusually poor prognosis.

It can be recognized roentgenologically by the demonstration of abnormal gas shadows in the region of the pancreas.

This is the 21st case reported in the literature.

Familiarity with this condition and awareness of the diagnostic roentgen findings may facilitate earlier recognition.

Dr. Leon Ginzburg gave us permission to report this case.

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Pneumatosis Cystoides Intestinalis with Intussusception

Report of a Case

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Comprehensive reviews[1,3,4,8] have discussed the literature and defined the terminology of pneumatosis cystoides intestinalis. Pneumatosis of the bowel is a rare condition with scattered cases being reported from all parts of the world. The lesion is seldom diagnosed before surgery, but a few have been found preoperatively by x-ray. The exact etiology of pneumatosis is not understood. The following case report adds to the literature by presenting the complication of intussusception in pneumatosis.

Report of Case

A 35-year-old married Spanish-American man was admitted on Sept. 10, 1958. He was entirely well until the morning of the day before admission, when he developed low abdominal pain, which persisted throughout the afternoon and during the night. Early on the morning of admission, the pain became much worse, at which time he consulted his doctor. The doctor felt that the patient had a ruptured appendix, and referred the patient to this hospital for treatment.

The patient had no associated symptoms except anorexia, and he had taken only sips of water by mouth. There was no nausea or vomiting, and no diarrhea. Just before the onset of the abdominal pain, the patient had a normal bowel movement.

Past history is not revealing. He had worked as a hard rock miner in the high mountains of Colorado most of his life. He served in the South Pacific during World War II; he denies having had any of the tropical diseases. He smokes less than one pack of cigarettes per day, and uses alcohol only occasionally. His family history is entirely negative. He had had the usual childhood diseases, but as an adult he has never been seriously ill. He has never had any surgery or serious injuries.

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Department of Surgery, Veterans Administration Hospital.

Physical examination revealed a fairly well developed and nourished male, who is of small stature. BP 110/70. Pulse 98. Temperature 99 F. Heart and lungs were normal. Examination of the abdomen revealed acute right lower quadrant tenderness to light palpation, and there was a palpable irregular mass in the right lower quadrant. There was slight muscle rigidity. Rectal examination elicited exquisite tenderness on the right side of the pelvis; otherwise it was negative.

Laboratory Examination.—Urinalysis was negative. Hemoglobin was 12.5 gm. %; hematocrit 42; WBC 20,450; neutrophils 87; stab forms 2, lymphocytes 11.

Course in Hospital.—With findings of a tender mass in the right lower quadrant and an elevated WBC, the patient was taken to surgery as an emergency, with diagnosis of acute appendicitis. With the patient under general anesthesia, the abdomen was opened through a right lower quadrant transverse incision. When the peritoneum was opened, a large irregular mass presented itself. The incision was enlarged, and further exploration revealed an ileocecal and cecal-cecal intussusception. This was readily reduced, and the appendix was now seen and was found to be only slightly edematous. Palpation of the cecum then revealed the presence of multiple soft tumor masses within the wall of the cecum. The masses could be palpated in the cecum and in the lower one-third of the ascending colon. Exploration of the abdomen revealed no further pathology. There were no enlarged lymph nodes in the mesentery, and the soft tumor masses described could not be felt in the upper portion of the ascending colon, transverse colon, or the descending colon. A resection was done to include the terminal 6 to 8 in. of the ileum, the cecum, and the lower ascending colon, beyond the extent of the tumor masses. An end-to-end ileocolostomy was performed. There was no gross contamination during the procedure, and the abdomen was closed without drainage.

After completion of the operation, the specimen was opened; the masses were incised, and were found to be cystic and contained gas. The specimen was sent to the laboratory for further pathology and x-ray examination. The resected

Figure 1

Fig. 1.—Resected bowel, showing the gas-filled cysts.

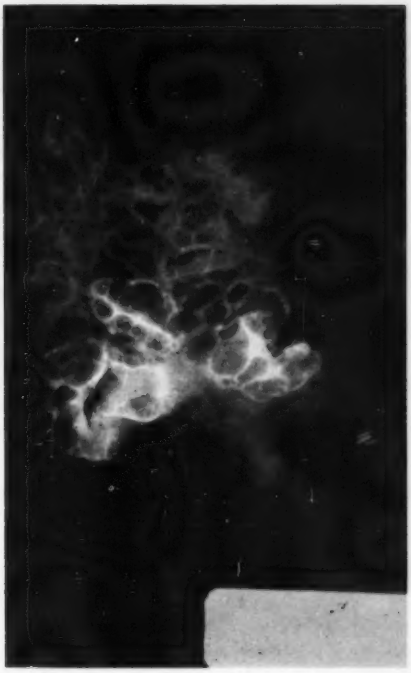
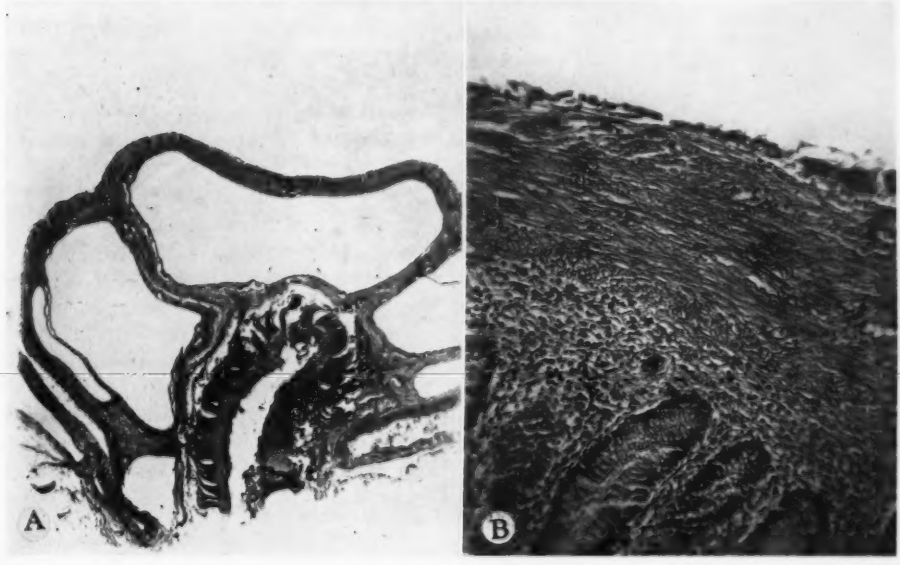


Figure 2

Fig. 2.—X-ray of the resected bowel.

Fig. 3.—Photomicrographs of cyst wall. *A*, reduced about 20% from mag. × 40. *B*, reduced about 20% from mag. × 200, showing typical foreign-body-like giant cells.



bowel showed typical gas-filled cysts (Fig. 1) which varied in size, measuring 4 to 25 mm. in diameter; microscopically the cysts were lined by foreign-body-like giant cells and a thin layer of granulation tissue, which was infiltrated with both acute and chronic inflammatory cells (Fig. 3). The appendix showed slight edema and a mild acute inflammatory cell infiltration. Figure 2 shows an x-ray view of the resected bowel.

The patient made an uneventful postoperative recovery, and he was released on the 13th day after surgery. An upper GI series done prior to discharge from the hospital showed no evidence of gastric or duodenal ulcer, tumor, or deformity.

On Nov. 12, 1958, the patient was seen in a follow-up. He was asymptomatic, and was having normal bowel movements. Follow-up flat plate of the abdomen at this time was negative for evidence of free gas or gas cysts of the intestines.

Comment

The interesting part of this reported case is the finding of the associated intussusception with pneumatosis of the cecum.

Reference to adult intussusception of any kind is somewhat sparse, and intussusception with pneumatosis is rare. Koss stated that Ciocca recorded one in 1933. Of Koss's group of collected cases (213) of pneumatosis 58% had associated stenotic lesions of the pyloric region; 15% of the cases were unassociated with any lesion; in the 15% group the cecum was frequently involved; the case presented would fit into this 15% group.

The diagnosis of adult intussusception is seldom made before operation, and in the presented case acute intussusception masqueraded as an acute appendicitis. Adult intussusception is associated with some specific organic lesion about 80% of the time [13]; our lesion was pneumatosis cystoides intestinalis. We cannot explain the pathogenesis of the pneumatosis; the patient was well nourished and we could find no preexisting pathology for this rare condition.

Summary

The second recorded case of intussusception in an adult due to pneumatosis cystoides intestinalis of the cecum and terminal ileum is presented.

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Ovarian Tumors in Childhood

Report of Six New Cases and Review of the Literature

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Ovarian tumors in children are not frequently seen. They comprise approximately 1% of all tumors found in children (Holt and McIntosh [1]). Although there are many elaborate classifications of ovarian tumors in adults, the principal ovarian tumors in children reported in the literature, in order of frequency, are ovarian cysts, teratomas, granulosa cell tumors, dysgerminomas, fibromas, embryonal carcinomas, and sarcomas. The latter were more frequently reported in the older literature, but were not all substantiated.

The first report of ovarian tumors in children was made by Wiel [2] in 1905, when he reviewed 60 case reports from the literature. This was increased to 86 by Downes [3] in 1921 and to 121 by Loeb and Levy [4] 11 years later. In 1937 Witzberger and Agerty [5] reviewed the world literature and found 186 cases of ovarian tumors in children up to and including 10 years of age. A review of the literature in 1958 revealed 71 additional cases of ovarian tumors in children, making a total of at least 257 cases reported up to this writing. To these we wish to add six additional cases from the Brooklyn Cancer Institute (now the John E. Jennings Hospital). These were included in 1954 in a report of 90 cases of tumors in children.[6]

The diagnosis of ovarian tumors in infancy and childhood could be greatly facilitated if such diagnosis were at least entertained as a possibility. However, the knowledge of tumors in children, especially ovarian tumors, is not widespread in the medical profession. It is therefore hoped that a review of the literature and a report of six additional cases will make physicians aware of this possibility.

The chief complaint in cases of ovarian tumors in infancy and childhood is a history of progressive abdominal enlargement, abdominal mass, and abdominal pain, acute, subacute or chronic. The pain is increased during periods of activity. It may be excruciating when there is torsion of the tumor pedicle, and may be associated with nausea, vomiting, high temperature, and high white blood cell count, giving the clinical picture of an acute surgical abdomen, including acute appendicitis. Pressure of the tumor on the ureters, bladder, and intestine may result in disturbance of urination and defecation. In some cases where the tumor fills the abdomen, or in the presence of ascites, there may be digestive and respiratory disturbance.

The granulosa-cell tumor is the principal feminizing ovarian tumor of childhood. Only about 10% of all granulosa-cell tumors occur in children under 16 (Hoffman and Wieczordwski).[7] This lesion secretes estrogen and is usually unilateral and of relatively low malignancy, as 70% to 80% follow a benign course (Anderson [8]). Clinically there will be a history of a whitish vaginal discharge followed by irregular bleeding and terminating in cyclic menstruation, regardless of the age of the child. However, ovulation does not occur. The breasts become enlarged, rounded, with prominent nipples and pigmented areolae; the vulva is hypertrophied. The uterus is enlarged; pubic and axillary hair will be noticed. Growth is accelerated, and the genitalia will have the appearance of a normal girl at puberty. According to Novak

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and Novak,[9] when such a tumor is removed, these clinical manifestations of precocious puberty promptly regress. They further state that instances are recorded in which, after removal of a unilateral tumor and disappearance of the abnormal symptoms, a recurrent tumor has developed in the remaining ovary with again the production of precocious pubertal symptoms and again their disappearance after removal of the second tumor. Similar clinical findings, except for the pelvic mass, may be observed in juvenile females affected by a tumor of the third ventricle (Dargeon[10]).

In children dysgerminomas may be associated with genital hypoplasia and pseudohermaphroditism. Microscopically this lesion resembles a seminoma of the testes and is histologically malignant. Clinically 20% to 30% of dysgerminomas are malignant, as judged by evidence of invasion and metastasis (Anderson[8]). Sterility is common. The tumor is very radiosensitive; hence there is less hesitancy in giving radiotherapy to this type of tumor when indicated. It usually occurs in children after 10 years of age. Bilateral ovarian tumors may be present in one-fourth of the cases. Unlike the granulosa-cell type, the tumor does not secrete hormones.

Teratoma of the ovaries is the commonest ovarian tumor in children. It is cystic or solid. The former is usually benign; the latter potentially malignant and responsible for more than half of the mortality due to ovarian tumors in children (Nelson[11]). The clinical history is not very revealing. Abdominal pain is less marked, sometimes absent, except in torsion of the pedicle, when the pain is excruciating. It is believed that ovarian teratomas in children are congenital in origin.

Ovarian fibromas are solid, slow-growing, benign tumors, usually unilateral, free from adhesions, and are notable for producing ascites when the diameter reaches 6 cm. or larger. They are at times associated with hydrothorax (Meigs syndrome). The latter sometimes may be erroneously interpreted as metastasis and considered as an inoperable malignancy. However, removal of the tumor results in disappearance of abdominal and pleural effusion (Dockerty and Masson[12]). The youngest case of ovarian fibroma in a series of 283 cases reported by Dockerty and Masson was 16 years old. According to Anderson, fibromas are not known to originate before puberty. (One of the cases to be reported here was 3 years old.) The tumor shifts position with the shifting of the body because of a long pedicle. After the first examination, the examiner may subsequently find the tumor on the opposite side of the abdomen, or the abdominal tumor may have disappeared and be wedged in the pelvis, producing pressure pain and resulting in disturbance of urination and defecation. Twisting of the pedicle, as in any other ovarian tumor, may produce the picture of an acute abdomen and require an emergency operation.

A good history alone may be suggestive enough to warrant a preliminary diagnosis of a "possible ovarian tumor." Inspection may reveal a visible abdominal mass. In most cases the uterus and its appendages are practically abdominal organs in infancy. Or the ovarian tumor may extend into the abdomen by a long pedicle. Hypertrophied breasts and genitalia, vaginal discharge or bleeding, mature appearance of the infant or child, or pseudohermaphroditism will all further suggest ovarian tumor.

Abdominal palpation may reveal the presence of a mass which may be the size of an orange or may fill the entire abdomen, or it may not be felt at all. In malignant tumors with metastasis, the liver may be enlarged and nodular. Multiple small tumors may be felt in addition to the large one. Ascites may be present. This is associated with cachexia, anemia, and loss of weight. If the tumor is within the pelvis, it may be detected by bimanual abdominorectal examination, or bimanual vaginal examination, under anesthesia if necessary.

A flat plate of the abdomen may show a dense, soft tissue shadow of the tumor.

Within the soft tissue shadow may be seen areas of calcification and portions of teeth or bone as seen in teratomas. A complete gastrointestinal series may show displacement of the intestines. Roentgenological skeletal survey may reveal precocious body growth with advanced bone age, early appearance and premature uniting of epiphyses, as seen in granulosa-cell tumors.

Chest x-ray should be taken in all cases of ovarian tumors to detect metastasis or Meigs syndrome. Further laboratory work may show a moderate increase of 17-ketosteroids and an enormous increase of estrogen.

Treatment

The treatment of choice for ovarian tumor in infancy and childhood is exploratory laparotomy. When the tumor is found to be unilateral with an intact capsule, without involvement of any other abdominal structure, conservative surgery, a unilateral salpingo-oophorectomy, will suffice, care being taken to prevent rupture of the capsule of the tumor with escape of its contents into the peritoneal cavity. Radiation therapy should be withheld, except in cases of dysgerminoma, in which sterility is common even without radiation and the tumor is radiosensitive. Radical surgery followed by radiation therapy is indicated if the tumor is bilateral or if a frozen section of the removed tumor proves it to be highly malignant, regardless of the type. Radiation therapy alone, chemotherapy, and hormone therapy are reserved for malignant tumors with widespread metastasis.

Careful follow-up of the patient with conservative surgery is even more important than with radical surgery. A "second look" and/or radiation therapy should always be kept in abeyance if indicated.

Ovarian tumor with a twisted pedicle is treated as an emergency the same as any other acute surgical abdomen. Care is taken that clamps are applied below the pedicle twist before manipulating the tumor to prevent distant embolization.

The prognosis of ovarian tumors in children depends on the degree of malignancy of the tumor, whether it is unilateral or bilateral, and whether regional or distant metastasis has already taken place.

Report of Cases

CASE 1.—*Malignant Teratoma with Intra-Abdominal Metastasis, Spontaneous Regression, Thirteen Years' Survival*

A 14-year-old girl was transferred to our Institution from another municipal hospital on Dec. 14, 1945, with a diagnosis of malignant teratoma of the right ovary with metastasis to the peritoneum and omentum. According to the history, the patient noticed that her abdomen was getting progressively larger. After an interval of two months she was taken to a doctor, who had her admitted to a city hospital with a diagnosis of "tumor of the ovary." On Nov. 31. 1945, an exploratory laparotomy disclosed a large tumor of the right ovary with numerous peritoneal and omental metastases. A right salpingo-oophorectomy and biopsies of the peritoneum and omentum were done. The tumor weighed 2,800 gm. The pathological diagnosis was "malignant teratoma of the ovary with metastases to omentum and peritoneum, the metastases consisting exclusively of neurogenic tissue."

The pathological diagnosis was confirmed by our pathologist as follows: "Section through the ovary presented a teratomatous lesion showing various elements, including some of ectodermal, entodermal and mesodermal origin. There was evidence of skin and accessory skin structures, central nervous tissue, respiratory, epithelial, cartilaginous, adipose and lymph tissue. Section through omental nodule showed the tumor tissue to be central nervous in type with numerous neuroglia cells in evidence." The final diagnosis was "teratoma of the ovary, malignant, with omental metastases."

The patient was treated symptomatically. Radiotherapy was withheld because "the tumor is radioresistant and the malignancy too far advanced." She was discharged to the Outpatient Department on Jan. 17, 1946, and was followed up at three-month intervals. She was last seen on Oct. 20, 1956, at the age of 25. She had been married, divorced, and remarried. She worked hard helping her husband, who was janitor of an apartment house. In August, 1958, she moved, leaving no forwarding address. However, a neighbor volunteered the information that the patient was "all right" when she moved away.

It was 13 years since the discovery of the malignant tumor with widespread metastasis to

the peritoneum and omentum, when, as the family put it, "she was given up to die."

This case emphasizes the importance of host resistance or immune reaction to cancer in patients with or without specific therapy, as brought out in another communication [13] in 1954.

Ewing [14] quotes the autopsy findings of a complete regression of peritoneal metastasis from a malignant teratoma of the ovary three years after laparotomy in an inoperable tumor. Fletcher [15] reports a case of papillary adenocarcinoma of the ovary with metastasis to the liver, with spontaneous disappearance of metastasis as shown by subsequent operation 29 months later. Dunphy [16] reports a case of inoperable carcinoma filling the pelvis, as shown by biopsy, with complete disappearance of the tumor nine years later.

CASE 2.—*Bilateral Malignant Dysgerminoma*

A 13-year-old girl was admitted to the hospital on Oct. 10, 1936, with the chief complaint of intermittent pain in the abdomen of two weeks' duration.

She had been a full-term infant, weighing 10 lb. (4,455 gm.) At the age of 2 years she had measles. At the age of 6 she developed a vaginal discharge, nonspecific in origin, which lasted for two years. Her hymen was incised and she received vaginal douches three times a day for a long period without any marked results. She had not menstruated up to the time of admission.

She appeared mature for her age. Her face was flushed, lips somewhat cyanotic. The pelvis and distribution of pubic hair were that of an adult female. There was a moderate amount of fine hair distributed over both thighs, upper lip, and lateral part of the face. There was also some fine soft hair on the abdomen and over the lumbosacral region. The hips were well padded with fat, and the breasts well developed.

The abdomen was enlarged. The liver extended three fingers below the costal margin. There was moderate tenderness in the right lower quadrant. No masses could be palpated abdominally. Vaginal examination revealed the whole pelvis to be filled with one solid mass.

The urine showed a slight trace of albumin. The blood Wassermann reaction was negative. The blood count showed a slight leukocytosis and a moderate secondary anemia. The vaginal smear showed both intra- and extracellular Gram-negative diplococci.

The chest roentgenogram was essentially negative. The intravenous pyelogram revealed a displacement of the right ureter medially by a large mass in the pelvis above the shadow of the bladder. The liver was seen to be enlarged about 3 in. below the right costal margin. Roentgenogram of the skull was negative.

At operation the peritoneum was found to be covered with small nodules. The peritoneal cavity contained about 10 to 15 oz. of sanguineous fluid. The whole pelvis was filled with multiple masses forming a solid, heavy roof over the uterus, which was small and not involved. A diagnosis of bilateral carcinoma of the ovaries was made. A liberal portion of the mass was removed for histological examination, and the abdomen closed in the usual manner. The patient made an uneventful recovery. Two weeks later the mother took the child home after she had been informed about the poor prognosis. The family moved soon after, and could not be traced. The removed tissue never reached the pathological laboratory. It was "lost in transit." In the light of our present knowledge, the clinical picture strongly suggests the diagnosis of malignant dysgerminoma.

CASE 3.—*Bilateral Carcinoma of the Ovaries with Generalized Abdominal Metastasis*

A 15-year-old girl was admitted to the hospital on Feb. 24, 1932, with the chief complaint of "swelling of her stomach." She stated that four months previously she noticed that her abdomen was getting progressively larger. She did not experience any pain or discomfort. Her mother became worried and brought her to the hospital.

She denied ever having been sick; however, she admitted that she had a "bad sore" on her lower lip followed by a swelling in her neck and a generalized rash all over her body. According to her mother the patient was born at full term, weighing 8 lb. (3,630 gm.), normal spontaneous delivery, breast fed. She had had whooping cough and measles. There was no record of the patient's menstrual cycle.

Physical examination revealed a 15-year-old Negro girl, not acutely ill, not in pain. Her temperature was 99 F, pulse 70, respiration 22, blood pressure 126/80. Her skin was covered with a macular, papular eruption with intervening old healed scars varying in size from a pinhead to a small pea. Head and neck examination was negative for pathology. Chest examination revealed a diastolic aortic murmur. The lungs were clear. The abdomen appeared large, globular, and tense (Fig. 1). A large, firm tumor appeared to arise from the pelvis, extending to the umbilicus. The tumor was fixed, firm and nodular, situated more to the left than to the right.

Vaginal examination revealed a large, irregular mass filling the entire cul-de-sac and pushing

Fig. 1. (Case 3).—Showing enlarged abdomen in bilateral carcinoma of the ovaries with generalized abdominal metastases.

forward the vaginal mucosa. The cervix was situated posteriorly and appeared normal on palpation, but could not be visualized. Rectal examination confirmed the vaginal findings of a pelvic tumor. The rectal mucosa was not involved.

The blood cell count showed a moderate secondary anemia. The white count was within normal limits. The urine showed a few pus cells, but was otherwise negative. The blood Wassermann was 4+. The chest x-ray was clear.

The patient received two blood transfusions of 500 cc. each, and on April 28, 1932, an exploratory laparotomy was performed. When the peritoneum was opened a great deal of straw-colored fluid came out under pressure. The whole omentum was studded with malignant nodules varying in size from a cherry to a hen's egg. The liver was covered with malignant nodules, as was the spleen. The pelvic organs were solidly fixed into one conglomerate solid mass inseparable from each other. One of the malignant nodules was removed for histological diagnosis, and the abdomen was closed in the usual manner. The postoperative diagnosis was carcinoma of the ovaries with widespread abdominal metastasis. The pathological report of the nodule was "metastatic carcinoma."

The patient remained in the hospital for one month, during which time she had to be tapped twice. Malignant cells were found in the fluid. The mother signed a release and took the patient home, where she died three months later.

CASE 4.—*Bilateral Carcinoma of the Ovaries in a Two-Year-Old Child*

A 2-year-old girl was admitted to our Institution on Nov. 3, 1930. Two weeks previous to admission she fell while running in the street. She immediately got up and complained of abdominal pain. However, she was up and about for six days without any further complaint of abdominal pain. On the sixth day she vomited. Her mother then brought her to our Hospital.

The patient was born at term, spontaneous delivery, weighing 5¾ lb. (2,610 gm.). She had been in good health until the present admission.

Physical examination revealed a 2-year-old white girl of a sallow, anemic, pasty appearance. Her temperature was 98.2 F, pulse 140, and respiration 24. The positive findings were an enlargement of the cervical, axillary, and inguinal glands. The tonsils were enlarged. There was a loud systolic murmur over the whole precordium. Abdominal examination revealed a tumor mass in each lower quadrant the size of an egg. Another mass was palpable below the umbilicus the size of a man's fist. All three masses were freely movable on palpation. The liver was enlarged to about one finger below the costal margin. The rest of the abdomen was soft. Several nodules were palpable through the abdominal wall.

The blood count showed a secondary anemia. The nurse called the intern's attention to the fact that the little 2-year-old girl was "menstruating." He replied that it was impossible, but did not take the trouble to find out, nor did he inform the visiting staff of the observation. Meanwhile no one would venture a diagnosis except "abdominal tumor." The patient received two blood transfusions of 350 cc. each and was scheduled for exploratory laparotomy. Operation disclosed bilateral carcinoma of the ovaries with general abdominal metastasis. Bilateral salpingo-oophorectomy was performed. The pathological report was "small cell embryonic carcinoma of the ovaries."

The patient remained in the hospital until Dec. 14, 1930, when the mother signed a release and took the child home, where she died on Feb. 12, 1931.

CASE 5.—*Carcinoma of the Ovary with Abdominal Metastasis*

A 15-year-old girl was transferred to our Institution from another municipal hospital on Dec. 19, 1930, with a diagnosis of "carcinoma of the left ovary with abdominal metastasis." The transcript of the hospital record revealed that in the summer of 1929 the patient was engaged in a fight with two other girls who kicked her and jumped on her abdomen. The mother of the patient noticed that the girl's abdomen was getting larger and became very hard during the following two weeks. The girl was taken to the hospital, where operation disclosed a tumor of the left ovary with metastases throughout the abdomen. A left salpingo-oophorectomy was done. The pathological report was medullary carcinoma of the ovary. She then received postoperative x-ray therapy and 4,000 mg. of radium pack to the pelvis. She also received radium pack to the upper mediastinum after x-ray disclosed a dense shadow in the superior mediastinum suggestive of metastasis.

On admission to our Institution the patient complained of abdominal pain, backache, and pain in the legs. Her past history revealed that she was born at term, normal delivery, weighing 13 lb. (5,895 gm.). Her postnatal condition was good. She had measles at the age of 3 years. Her first menstrual period was at the age of 12. She had not menstruated since she received x-ray therapy. On admission she weighed 90 lb., having lost 28 lb. since her illness.

Physical examination revealed a 15-year-old girl, chronically ill, emaciated, anemic, very nervous and noncooperative. Her temperature was 99.2 F, pulse 110, respiration 24, blood pressure 110/70. The abdomen was markedly distended and tympanitic, with clinical evidence of intra-abdominal fluid. The liver was enlarged about three fingers below the costal margin. The spleen was not palpable. A hard, tender mass was felt in the epigastrium.

A gastrointestinal series revealed no intrinsic pathology of the gastrointestinal tract. X-ray of the chest showed no metastasis. The blood cell count showed a moderate secondary anemia. The histological diagnosis of carcinoma of the ovary was confirmed at our Institution. The patient remained in the hospital under supportive treatment and died Jan. 20, 1931. Consent for an autopsy could not be obtained.

CASE 6.—*Fibroma of the Ovary in a Three-Year-Old Child*

A 3-year-old girl was admitted to the hospital on Dec. 12, 1951, with a six weeks' history of abdominal pain. Six weeks prior to admission she developed pain in the right lower quadrant associated with diarrhea. The family doctor was called and noted a mass in the right lower abdomen. She was then admitted to the hospital. Her past history and family history were essentially negative.

Physical examination on admission showed a 3-year-old, well-developed, well-nourished Negro girl, who appeared twice her age. There was a tumor mass the size of a large grapefruit arising from the pelvis palpable above the symphysis pubis. It was firm, somewhat irregular, freely movable, and not tender to palpation. The liver and spleen were not palpable. The rest of the physical examination was essentially negative.

Roentgen examination of the chest was negative. A flat plate of the abdomen and an intravenous pyelogram showed a gaseous distention of the entire colon with the exception of the

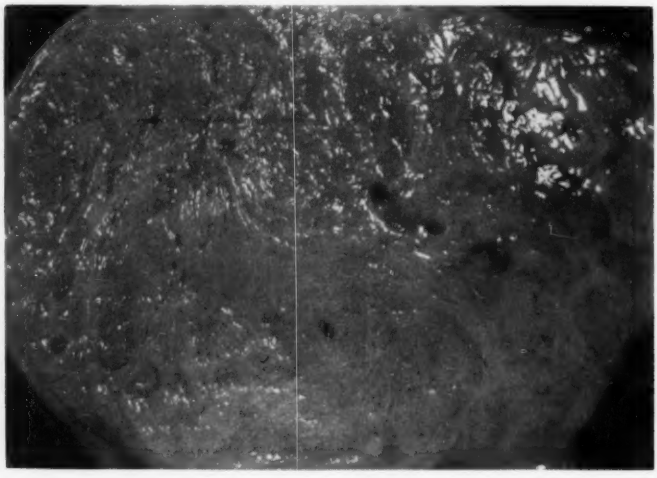

Fig. 2 (Case 6).—Cross section of tumor showing fibroma of ovary, calcification, and myxomatous changes.

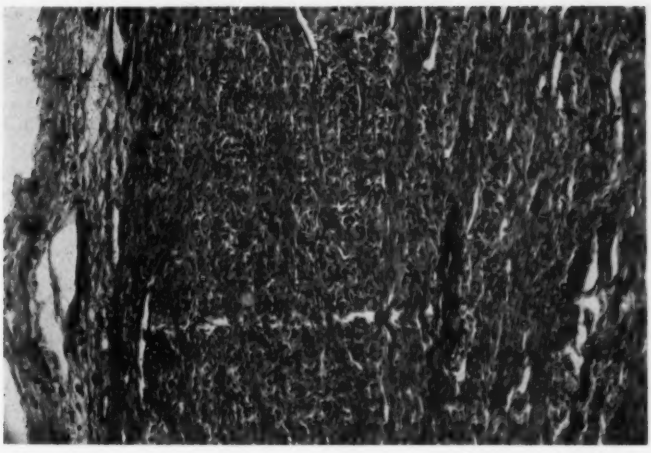

Fig. 3 (Case 6).—Photomicrograph, reduced about 32% from mag. × 220, showing fibroma of the ovary.

sigmoid portion, which was obscured by a homogeneous, moderately dense opacity occupying the periumbilical area. This was interpreted as an ovarian teratoma or dermoid cyst. The genitourinary tract was negative for pathology. The urine, blood count, blood chemistry, and Wassermann test were negative.

On Jan. 2, 1952, at operation a large tumor the size of a grapefruit was found in the lower midabdomen, attached to the left Fallopian tube by a long pedicle twisted twice upon itself (Fig. 2). The surface was irregular with many dilated veins anteriorly and posteriorly. The right tube and ovary appeared normal, and there was no other tumor in the pelvis or abdomen. The liver and spleen appeared grossly normal. The tumor and left Fallopian tube were double-clamped below the twisted area and removed. On section the whole tumor seemed to arise from a small structure measuring about 2 cm. in diameter, which grossly appeared to be ovary. The pathological report was "fibroma of ovary with myxomatous changes and calcification" (Fig. 3).

The patient made an uneventful recovery and was discharged on Jan. 17, 1952. She was last seen on Dec. 21, 1958. She was in good physical condition, with no evidence of recurrence. She weighed 106 lb. and appeared very happy, with no complaint.

Summary

Ovarian tumors in children are not frequently seen. Such a possibility is seldom considered in a differential diagnosis of "abdominal mass." The literature on the subject is reviewed; diagnosis and treatment are discussed, and six new cases are reported. It is hoped that this paper will help to facilitate the study of ovarian tumors in children.

75 Prospect Park S.W. (15).

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Traumatic Diaphragmatic Hernia

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Hernias of the diaphragm can be divided into two major groups, those which are nontraumatic and include hiatus hernia, Morgagni hernia, and hernia of Bochdalek, and those which are traumatic in origin. Traumatic diaphragmatic hernias may further be subdivided into those which are caused by direct trauma to the diaphragm and those caused by indirect trauma. Direct trauma usually results from stab or gunshot wounds wherein the diaphragm is actually penetrated by the traumatic incident. Indirect trauma is commonly associated with severe injuries to the abdomen or chest secondary to high velocity or industrial accidents. The bursting effect secondary to the sudden compression of the lower chest or upper abdomen causes a rent in the diaphragm with herniation of the abdominal contents into the chest cavity. A rare cause of traumatic diaphragmatic hernia is the rupture through this structure of a contiguous inflammatory mass such as a subphrenic abscess.

Since traumatic diaphragmatic hernias have no peritoneal sac, they allow herniation of any freely mobile abdominal viscus into the lower chest. The common organs thus involved include the stomach, colon, and small intestine. These hernias usually involve the left diaphragm since the liver protects the right diaphragm. Occasionally, however, a traumatic herniation of the right diaphragm can occur, in which case the liver may occupy the right lower chest.

There are two main dangers or hazards in traumatic diaphragmatic hernia. The early one is frequently caused by pressure on intrathoracic organs caused by the herniating abdominal ones. In such cases, acute deviation of the mediastinum may cause shock and even sudden death. Cyanosis, dyspnea, and circulatory collapse are commonly seen. The later hazards are those of the effects of the herniation on the organs herniating. Obstruction, strangulation, and vague abdominal pains may be a part of this picture.

Carter describes three phases of a typical traumatic diaphragmatic hernia. The first of these is the so-called acute phase occurring in the period directly after the accident. This phase may be obscured by other serious injuries occurring at the same time as the hernia. Its severity varies with the pressure exerted on the intrathoracic organs by the herniating mass. Shock, upper abdominal pain, shoulder pain, dyspnea, and cyanosis may occur. Physical signs are frequently sufficiently altered to allow diagnosis on the physical examination of the chest alone. Diminished excursion of the ipsilateral thorax, impairment of resonance, mediastinal displacement, and adventitious sounds in the chest are oftentimes found. An x-ray of the chest may show one or all of the following findings: gas and fluid pockets in the chest, an abnormally elevated diaphragm, mediastinal shift to the contralateral side of the lesion, and pleural effusion.

If the diagnosis of traumatic diaphragmatic hernia with abdominal viscera in the chest is suspected, confirmation can often be made by passing a Levin tube into the stomach and then making another chest x-ray. The tube often can be demonstrated in the thorax by such an x-ray. Likewise, an emergency barium enema may show the colon in the chest and help establish the diagnosis.

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When discovered in the acute phase, the surgical repair of a traumatic diaphragmatic hernia is often an emergency. Exploration should be carried out as soon as the patient is prepared from the general standpoint. Many times correction of the hernia must be done before the cyanosis, dyspnea, and other mechanically caused aberrations can be corrected.

It must be emphasized that other concomitant injuries often mask the discovery of the traumatic diaphragmatic hernia. The following case illustrates this fact.

CASE 1.—A 30-year-old Negro woman was in an auto accident at 1:30 a. m. on April 22, 1954. She was admitted to Carle Hospital somewhat later in shock with fractures of both femurs and multiple lacerations about both legs. She complained during the next few days of abdominal pain, but this gradually subsided. Chest examination at this time was negative. Between the first admission in April, 1954, and the hospital admission of January, 1956, the patient had multiple orthopedic procedures with eight anesthesias. On Jan. 11, 1956, she was admitted for removal of a sequestrum of the left femur. Because of anesthesia difficulties, however, the patient was returned to her hospital bed and a chest film ordered. This revealed most of the stomach to be in the left chest, as well as some of the colon and small intestine (Figs. 1 and 2). A Levin tube was immediately inserted into the stomach and 1,000 cc. of fluid and a large amount of air evacuated. This improved the patient's condition almost immediately. The diagnosis of traumatic diaphragmatic hernia was made. Transthoracic exploration was carried out on Jan. 18, 1956, and the entire stomach, first portion of the duodenum, transverse colon, and several loops of small bowel were found in the left chest. The rent in the diaphragm was approximately 8 cm. in diameter. The repair of the hernia was successfully carried out.

If a traumatic diaphragmatic hernia escapes detection during the immediate post-

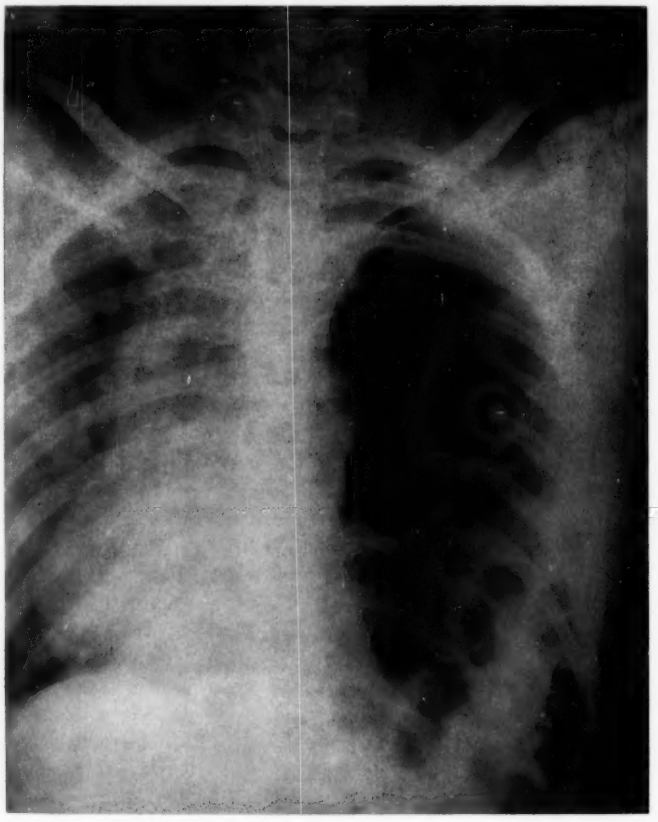

Fig. 1.—Anteroposterior view of the chest. Note that the entire left chest is filled with stomach, large and small intestine. The mediastinum is markedly shifted to the right.

Fig. 2.—A lateral view following barium ingestion reveals that almost the entire stomach occupies the left pleural space.

injury, or so-called acute phase, the second or interval phase is entered. This phase may last a varying period of time, but usually is one to three years in duration. During the interval phase, vague abdominal symptoms are often manifest that are mistaken for other intra-abdominal conditions, as peptic ulcer, gallbladder disease, or irritable bowel. Bouts of mild intestinal obstruction may prompt abdominal studies that disclose the hernia. A routine chest x-ray may also show findings much as those mentioned in the acute phase that prompt suspicions of diaphragmatic hernia. If the diagnosis of traumatic herniation of the diaphragm is made in the interval phase, surgical therapy should be advised on an elective basis because of the chance of subsequent obstruction or intestinal strangulation. The following case is one discovered during the interval phase with subsequent successful surgical management.

Case 2.—A 48-year-old white woman was seen at Carle Clinic on March 2, 1949, because of gaseous abdominal distention of many years. Her past history revealed that she had had a gunshot wound in the left flank, involving the flank and lower chest, some 20 years previously with a very slow postoperative recovery. This gunshot wound, it was further discovered, was self-inflicted by the patient. Abdominal symptoms were relieved by standing or belching. The chest x-ray revealed the gastric air bubble to be occupying the left

lower chest with compression of the left lung and displacement of the mediastinum to the right. A gastrointestinal x-ray series showed two-thirds of the stomach to be in the left chest with the stomach inverted and reaching as high as the third rib anteriorly. The diagnosis of traumatic diaphragmatic hernia was made, and on March 26, 1949, exploration of the left chest was carried out. Most of the stomach was found in the left chest and the opening in the middle of the dome of the diaphragm was approximately 6 cm. in diameter. No strangulation or evidence of obstruction was present. The defect was successfully closed and the patient made a very uneventful recovery. Follow-up x-rays were made on July 1, 1954, which showed the diaphragm and left chest to be entirely normal. At this time the patient was asymptomatic.

The third and final phase of a traumatic hernia of the diaphragm is that of intestinal obstruction or strangulation. This phase may be ushered in by several bouts of partial intestinal obstruction or may suddenly start with a complete intestinal obstruction with or without evidence of intestinal strangulation. Cramping abdominal pain, abdominal distention, dyspnea, cyanosis, and severe toxicity may be a part of the picture. Hematemesis can occur if the stomach is strangulated in the chest. Likewise bloody stool per rectum may occur if the colon's blood supply is seriously compromised. The true etiology of an obvious intestinal obstruction may be overlooked if the examiner is not on guard for the possibility of diaphragmatic hernia as a cause. A recent case brought this fact to our attention.

CASE 3.—A 74-year-old white man was first seen at the Carle Clinic on Jan. 31, 1958, with a severe abdominal distention, dehydration, and intestinal obstruction of four days' duration. Emergency x-rays of the abdomen showed marked distention of the right and transverse colon. The

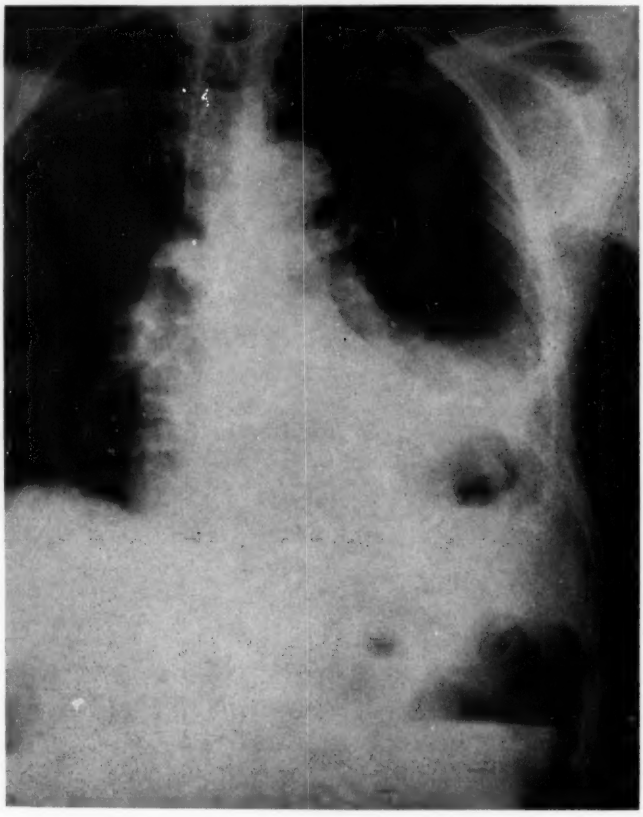

Fig. 3. — Posteroanterior chest film reveals pleural thickening and fluid levels in the left lower chest. There is a suggestion of a hollow viscus occupying a supradiaphragmatic position on the left.

diagnosis of closed loop colon obstruction was made, and, after adequate hydration, a loop colostomy was done under local anesthesia. The patient's condition was critical and he had an exceptionally stormy postoperative course with urinary retention and intermittent abdominal distention. Preoperative chest x-rays revealed a marked elevation of the left diaphragm with old rib fractures and a fluid level or pleural thickening at the left base (Fig. 3). On Feb. 14, 1958, a barium enema was done, which revealed the splenic flexure of the colon to be in the left chest. Further history now revealed that the patient had fallen off a ladder two years previously and struck the left lower chest, with uneventful recovery. There had been no intervening symptoms. A diagnosis of traumatic diaphragmatic hernia was made and transthoracic repair carried out on March 3, 1958. The left transverse colon occupied the left chest plus 200 cc. of serosanguineous fluid. The rent in the diaphragm was 7 cm. in diameter. This defect was closed, and the patient made an uneventful recovery. The colostomy was closed on March 17, 1958. He is at present in good health.

Not all cases of the third phase of traumatic diaphragmatic hernia are as cryptic as the one just presented. Many times in the past the accident has been severe enough to immediately divert the examiner's attention to the true etiology of the intestinal obstruction and abdominal findings. The following case is illustrative of this.

CASE 4.—A 22-year-old white man was admitted to the Carle Hospital on Feb. 11, 1957, because of four days of cramping abdominal pain with associated abdominal distention and daily vomiting. Past history revealed that he had been involved in a severe auto accident six months previously with left rib fractures, collapsed left lung, and pleurisy on the left. No intestinal problems had occurred at that time. He had been hospitalized for one week and then dismissed.

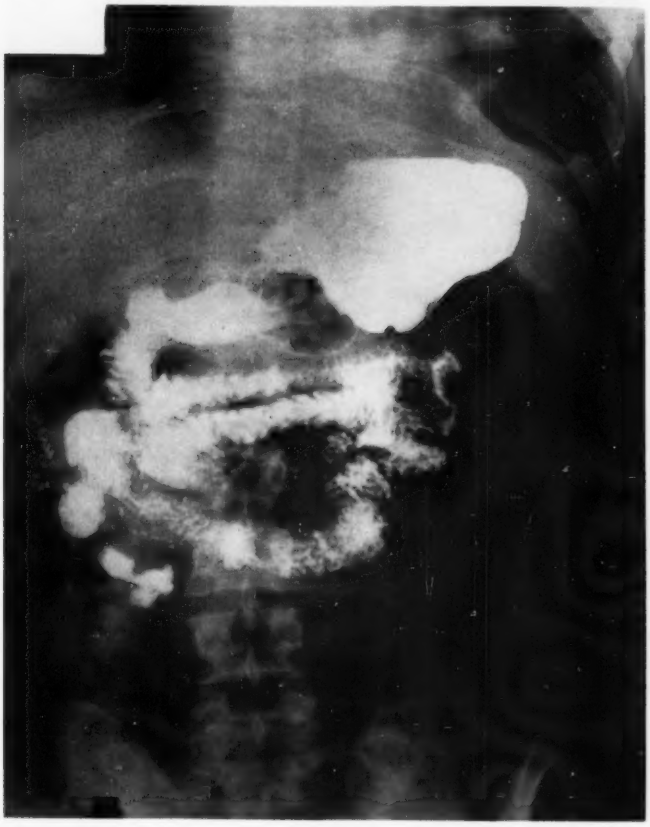

Fig. 4.—Barium study of the stomach reveals that it is in a normal position and suggests that the colon occupies the left lower chest.

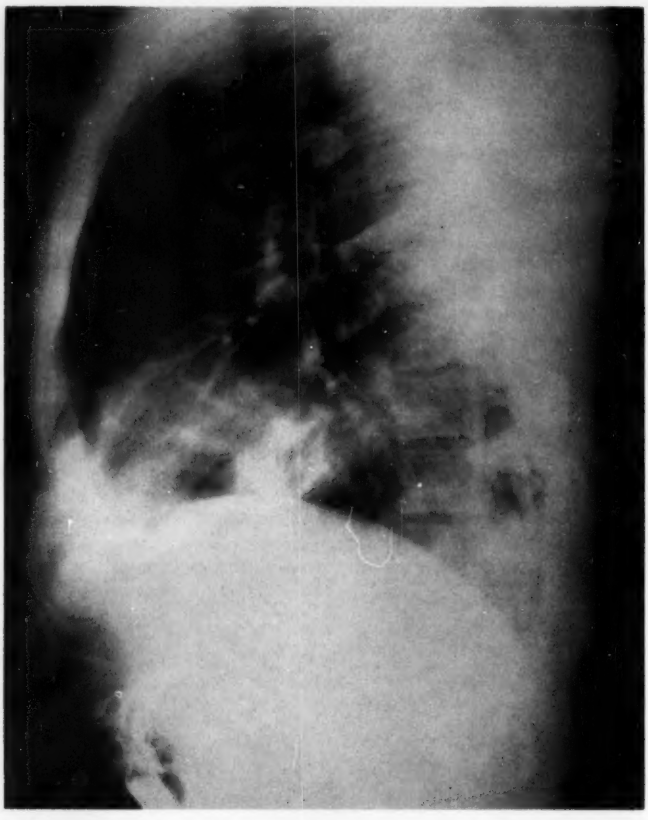

Fig. 5.—Lateral roentgenogram of the chest reveals a large viscus occupying the left lower chest. This was later proved to be the colon by barium enema studies.

X-rays here showed that the stomach was in a normal position and suggested that colon occupied the left lower chest (Figs. 4 and 5). A barium enema revealed the splenic flexure of the colon to be located in the left chest. After proper preparation, surgery was carried out as an emergency and 800 cc. of serosanguineous fluid was found in the left chest plus the splenic portion of the colon and a large piece of omentum. The hernial ring measured 6 cm. in diameter. Repair of the hernia and reduction of the stomach were carried out uneventfully. Postoperatively the patient did well and he was dismissed on the ninth postoperative day. Follow-up study six months after the operation revealed the left diaphragm and chest to be entirely normal.

Surgical Treatment

When the diagnosis of traumatic diaphragmatic hernia has been made, surgical correction of the hernia is advisable because of the dangers of strangulation and obstruction, as well as of undue pressure on intrathoracic organs. This does not mean that surgery should be carried out even in the face of other severe injuries or the presence of hemorrhagic shock. The surgeon must be sure, however, that the critical condition of the patient is not caused by the hernia itself. In such cases, the passage of a stomach tube into a herniated stomach may release enough gas and fluid to reduce intrathoracic pressure and temporarily improve the patient's condition. Even if a traumatic diaphragmatic hernia is discovered in the relatively symptomless or interval phase, surgery should be advised at the patient's early convenience because of the aforementioned dangers.

A posterolateral thoracic incision through the bed of the resected seventh or eighth

rib is our choice. This gives the surgeon adequate access to the diaphragm and the defect in the diaphragm through which the herniating organs pass. Adhesions of the ring of the diaphragmatic defect to the herniating viscera are common, and since there is no hernial sac present, great care must be exercised in dissecting out the hernial ring. The operator should not hesitate to open the defect in the diaphragm radially at any point in order to insure adequate exposure. Before reduction of the herniated organs back into the abdomen, a meticulous examination is made to make certain that no compromise has occurred to the circulation of these organs. If infarction is present, resection will be necessary. In such instances it is advisable to extend the incision into a thoracicoabdominal one, crossing the costal margin. The chest can then be packed off with sterile packs and the intestinal anastomosis carried out within the abdomen. This maneuver may help prevent postoperative empyema. Closure of the diaphragmatic defect is then carried out after debridement of its margins. Interrupted figure-of-eight sutures of No. 0 silk are used for this closure, and these sutures are supplemented by a running suture of No. 00 silk. The chest is then lavaged with sterile saline and the lung carefully reexpanded. A catheter is left in the posterior gutter through a stab wound in the ninth interspace for 24-48 hours of closed intercostal drainage. The chest wall is closed in a routine fashion. Phrenic nerve crush, although advised by some authors, is not carried out routinely by us. A large defect with some tension on the closure certainly would be an indication for phrenic crush. In the case of a small defect that closes easily, and particularly in older persons in whom an effective postoperative cough is important, phrenic crush is not done.

The postoperative care is similar to that for other thoracic surgical cases. If intestinal resection is necessary, the usual postoperative management is added for the intestinal anastomoses.

Summary

Traumatic herniation of the diaphragm is becoming a commoner lesion with the increasing frequency in occurrence as a consequence of highway and other violent accidents. A discussion of symptomatology, findings, and surgical treatment of traumatic diaphragmatic hernia is given, along with four surgically treated cases that exemplify the various phases of this unique lesion.

Carle Hospital Clinic.

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An Evaluation of Pancreatic Biopsy with the Vim-Silverman Needle

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Usually an experienced surgeon can identify correctly the nature of a mass in the pancreas by inspection and palpation. The consistency of the lesion, presence or absence of involvement throughout the pancreas, evidence of inflammatory reaction, presence of calcification or fat necrosis, existence of lymphadenopathy in the vicinity, secondary effects of the pancreatic lesion on the biliary tract, and evidence of extension of the process to surrounding tissues aid in establishing an accurate diagnosis. In addition, the patient's age and history and the results of preoperative clinical investigation may provide important leads to the diagnosis prior to laparotomy. On the other hand, even the experienced surgeon may have difficulty at times in determining the exact nature of a lesion in the pancreas by gross findings alone. Appropriate surgical treatment of the lesion usually requires an exact diagnosis, as is true with other surgical lesions.

Errors in surgical diagnosis of pancreatic lesions have been reported to vary from 17% to 23%.[1,2] Fraser,[1] in 1938, reviewed a collected series of 1,035 cases of obstructive jaundice related to disease in the pancreas. Cases of acute pancreatitis and biliary lithiasis were excluded. He found that the pancreatic process was malignant in 74% of the cases and benign in 26%, on the basis of a follow-up study of two years. In his study the lesion in the pancreas was diagnosed at operation as being malignant in 7% of the cases in which only inflammatory disease was actually present. In addition, in 16% of the cases in which a malignant disease was actually present, the diagnosis of an inflammatory lesion had been made.

Pancreatic biopsy of wedge-type specimens has been used infrequently in the past.[1-3] The difficulty of securing adequate pancreatic tissue,[4-7] the frequency of hemorrhage,[2,8,9] the possibility of creating a pancreatic fistula,[3,8,10] the difficulty of interpreting frozen sections in pancreatic cancer,[4-6,10,11] the high incidence of misleading and false impressions obtained from biopsies,[3,8,11,12] and the danger of malignant implantation[7] are among the main reasons why this type of specimen has not been used more frequently for biopsy. Probstein and associates[3] studied wedge-type specimens of pancreas and found malignant lesions in only 43% of 23 known cases of pancreatic neoplasm. In a similar series of patients who had far-advanced pancreatic carcinoma Child[13] reported positive evidence at biopsy in 60% of the wedge-type specimens.

There have been few reports of use of the Vim-Silverman needle for obtaining pancreatic specimens for biopsy. Kirtland[14] in 1951 referred to the safety of this procedure. Crile and Vickery[15] in 1952 reported its use in 11 cases. About 10 years ago we became interested in the Vim-Silverman needle as a means of obtaining specimens of pancreatic lesions for biopsy. It was recognized as an aid in differential

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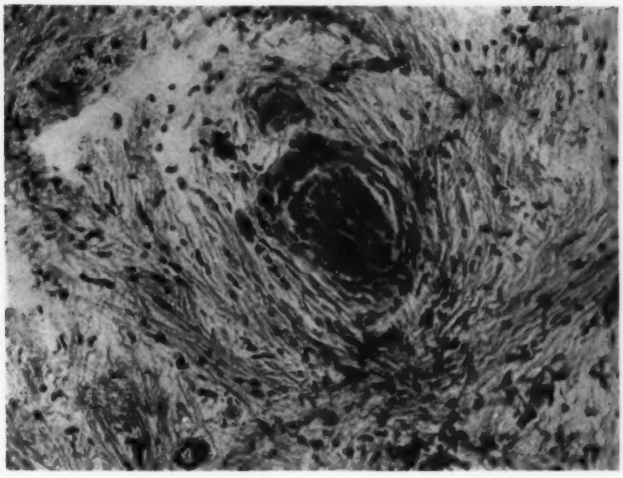

Fig. 1.—Grade-2 scirrhous adenocarcinoma. The presence of perineural growth of epithelial cells makes certain the diagnosis of cancer. This can be a most useful observation in certain borderline cases (Vim-Silverman needle specimen; hematoxylin and eosin; × 200).

diagnosis, especially in the patient in whom gross findings at the time of operation left reasonable doubt concerning the true nature of the lesion.

Present Study

Our study was undertaken to evaluate the experience that we have had with biopsy of pancreatic specimens obtained with the Vim-Silverman needle, particularly from the viewpoints of adequacy of the specimen, accuracy of diagnosis on study of frozen sections and usefulness and safety of the needle.

Specimens were obtained from the pancreas with the Vim-Silverman needle in 99 patients during exploratory laparotomy between April, 1949, and December, 1954. Specimens were taken only from patients who had a mass in the pancreas. In three cases peritoneal implants were noted, and in one metastatic nodules were found in the liver. These four cases were excluded from the study, as were two others in which conventional methods of biopsy disclosed the presence of carcinoma originating from the common bile duct. Later 10 additional cases were deleted because no information

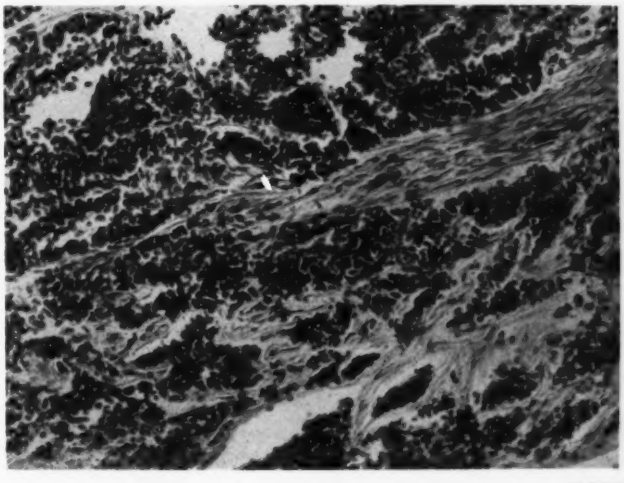

Fig. 2.—Small-cell carcinoma, Grade 4, of pancreas as revealed by the Vim-Silverman needle biopsy technique (hematoxylin and eosin; × 175).

Fig. 3.—Pancreatic lymphosarcoma, lymphoblastic type; Vim-Silverman needle specimen (hematoxylin and eosin; × 175).

was available concerning the course of the patients' disease in the follow-up studies. Eighty-three cases, therefore, were used in the present study. The specimens used for biopsy measured 1 mm. in diameter and 2 to 6 mm. in length. An average of three or four slides for microscopic study by the fresh-frozen section technique [16] were prepared from each specimen. In addition, fixed sections also were prepared in 75 of the 83 cases.

For purposes of comparison, wedge-type specimens of pancreas from 110 cases in which biopsy had been performed between the years 1935 and 1955 were reviewed. This group likewise represented cases in which a pancreatic mass had been identified during exploration. No case of neoplastic involvement of lymph nodes, metastasis to the liver, or peritoneal implants was included in this group. The condition of each patient in both series was followed for at least three years.

Results of Biopsy of Pancreatic Specimens Obtained with Vim-Silverman Needle

Histologic Findings.—A malignant lesion was diagnosed on histologic study of speci-

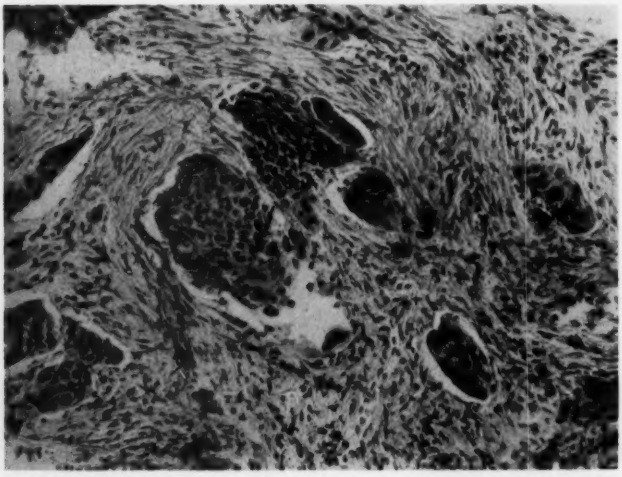

Fig. 4.—Grade-3 epidermoid carcinoma—a rare but well-recognized type of primary pancreatic neoplasm (Vim-Silverman technique; hematoxylin and eosin; × 150).

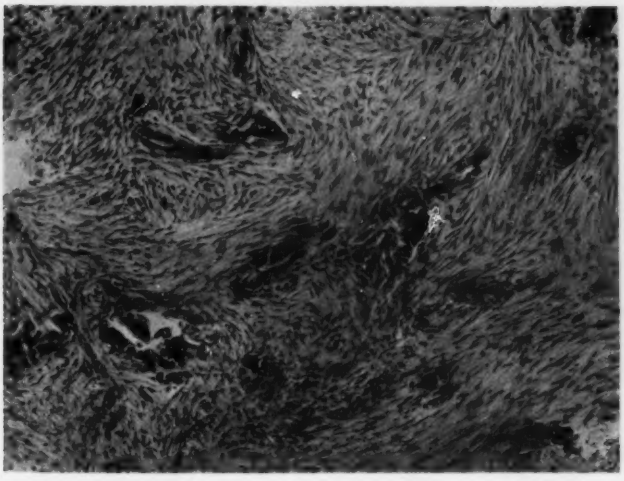

Fig. 5.—Grade-3 scirrhous adenocarcinoma. Superficially this bears some slight resemblance to chronic pancreatic fibrosis, but the manifest anaplasia of the epithelial cells becomes obvious under higher objectives of the microscope (Vim-Silverman needle specimen; hematoxylin and eosin; × 150).

mens of pancreas taken with the Vim-Silverman needle in 36 of the 83 cases. In each of the 36 cases there was adequate tissue to identify the type of lesion present and to permit grading by Broders' method.[17] In 32 of the 36 cases there was adequate tissue to permit preparation of fixed specimens as well as frozen sections. The diagnosis made on study of each of these permanent sections verified the diagnosis made on study of the frozen section. The diagnoses in the 36 cases in which a malignant lesion was found were as follows: adenocarcinoma in 34 (Figs. 1 and 2), lymphosarcoma in one (Fig. 3), and squamous-cell carcinoma in one (Fig. 4). Of the 34 adenocarcinomas, 12 were Grade 4, 11 were Grade 3, 10 were Grade 2 and 1 was Grade 1; 24 were classified as scirrhous in type (Figs. 1 and 5), three as mucous (Fig. 6), three as large-cell, two as small-cell (Fig. 2) and one as adenoacanthoma. The single Grade-1 lesion was not classified further. Occasionally perineural lymphatic infiltration was noted in the specimens (Fig. 1). Perhaps it would have been noted more frequently had not most of the specimens been taken by inserting the

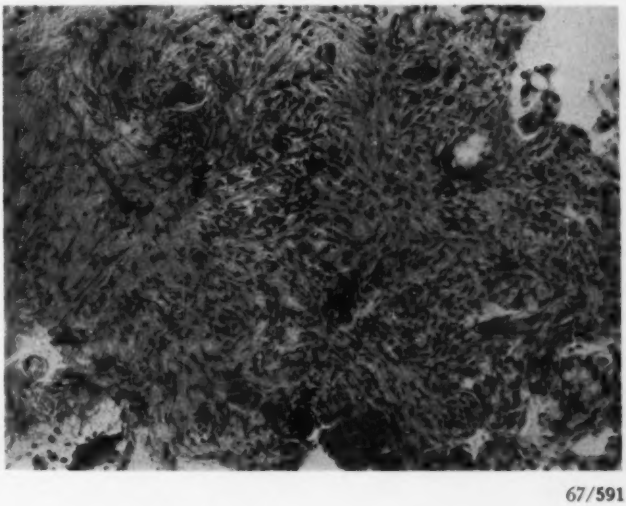

Fig. 6.—Isolated clusters of signet cells is a Grade-3 mucous adenocarcinoma of the pancreas (Vim-Silverman needle specimen; hematoxylin and eosin; × 150).

needle into the anterior surface of the pancreas.

The other 47 of the 83 specimens of pancreas obtained with the Vim-Silverman needle were reported to show normal pancreatic tissue, a benign pathologic process, or an inflammatory reaction on study of frozen sections. Satisfactory permanent slides were prepared in 43 of the 47 cases. Microscopic study of these slides resulted in a diagnosis which was identical with that which had been made on study of the fresh-frozen section in each case. In the remaining four cases, so-called preserved frozen sections, that is, sections which had been placed in formalin, destained, and restained with hematoxylin and eosin, were reviewed, but no change was made in diagnosis.

Forty of the benign specimens showed evidence of chronic pancreatitis. Minimal to pronounced increase in fibrous connective tissue, either interlobular or intra-acinar in location, and with or without lymphocytic infiltration, was present in all of these specimens. The findings corresponded to what Bell [18] has termed "interstitial pancreatitis." Also included as specimens of chronic pancreatitis were those which revealed marked fibrous reaction, lymphoplasmocytic infiltration, and atrophy of the pancreatic parenchyma with dilatation and squamatization of the ductal system.

In addition, focal areas of fat necrosis (Fig. 7) and calcification were present in some specimens. It is well known that a carcinoma of the pancreas is usually surrounded by pancreatic tissue which evidences changes of chronic pancreatitis. The degree and extent of such changes vary considerably from patient to patient. Changes of this type were found on initial biopsy in some patients in whom a second or third specimen revealed carcinoma. Initial specimens which evidenced chronic pancreatitis are not included in the group of benign cases if subsequent specimens showed evidence of malignant disease.

In one case, multiple biopsies of a mass which involved the head of the pancreas and measured 12 cm. in diameter disclosed a subacute inflammatory reaction. Subsequently the patient died and the diagnosis of subacute pancreatitis was verified at necropsy. In six cases in which lesions were benign only normal pancreatic tissue without any evidence of pathologic change was found.

Clinical Verification of Histologic Findings.—The three-year follow-up was carried out either by reexamination or by letter. All 36 patients in whom a diagnosis of malignant lesion was made on evidence found at biopsy died within the first year after operation. The average length of post-

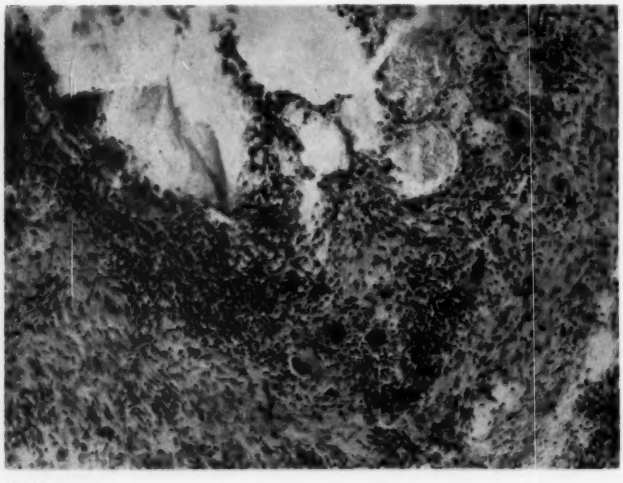

Fig. 7.—Subacute chronic pancreatitis featuring fat necrosis and an inflammatory infiltrate with foreign-body giant cells (Vim-Silverman technique; hematoxylin and eosin; × 125).

operative life was five and a half months. While necropsy reports are not available in many cases, the patients' clinical courses were such that there is little doubt in any case regarding the existence of a malignant lesion in the pancreas. It appears, therefore, that a positive diagnosis of malignant disease made on study of a frozen section prepared from a specimen of pancreatic tissue obtained for biopsy with a Vim-Silverman needle is very reliable if the pathologist is experienced in the study of such preparations.

Of the 47 patients in whom no evidence of a malignant lesion of the pancreas was detected on biopsy, 28 lived for more than three years after operation. Two additional patients died within this three-year period, but necropsy, which was performed in each case, did not reveal a malignant lesion. We can be reasonably certain, therefore, that 30 of these 47 patients did not have a malignant lesion in the pancreas. The remaining 17 patients died within three years after operation, with an average survival of seven and a half months. The longest survival in this group was 15 months. Necropsy was not performed in all 17 cases, and it is possible that not all patients had a malignant lesion of the pancreas; but, if it is assumed that they did, the accuracy of diagnosis by biopsy of the pancreas with the Vim-Silverman needle in this entire group of 47 patients would be approximately 64%.

Results of Biopsy of Wedge-Type Specimen of Pancreas

A similar study was made of 110 cases in which wedge-type specimens of pancreas were taken for biopsy from patients who had a mass in the pancreas but in whom there was no distant objective evidence of neoplasm. In other words, the gross findings at the time of operation among these patients were similar to the findings among patients in whom specimens for biopsy were taken with the Vim-Silverman needle. In this group also, follow-up study for at least three years after operation was carried out either by reexamination or by letter.

In 26 of the 110 patients a malignant lesion was diagnosed on biopsy of the specimen. The subsequent course of each of these patients indicated that death was due to a malignant growth. The average length of postoperative life was four and a half months.

In 84 of the 110 patients, no evidence of a malignant lesion was found in the specimen obtained for biopsy. Of the 84 patients, 50 survived more than three years after operation. An additional four patients died within three years after operation, but no malignant lesion was found at necropsy. The remaining 30 patients in this group of 84 died within three years after operation. In 4 of the 30 patients necropsy findings revealed malignant lesions in the pancreas, and malignant lesions of the pancreas were strongly suspected from the clinical course in the remaining 26 patients in this group. If it is considered that death of these 30 patients was due to malignant lesions of the pancreas, the accuracy of diagnosis in the 84 patients in whom biopsy did not reveal a malignant lesion was 64.2%.

Comparison of Findings in Biopsies of Wedge-Type Specimens and Those Taken with Vim-Silverman Needle

If an attempt is made to compare findings of pancreatic biopsy depending on the manner in which the specimen for biopsy was taken, certain assumptions become necessary: (1) that the material comprising the two groups was similarly selected, (2) that any patient who lived more than three years after operation did not have a malignant lesion of the pancreas, and (3) that any patient who died within three years after operation, unless necropsy revealed otherwise, did have carcinoma of the pancreas. Obviously, when such assumptions are necessary, this study does not have the advantage of completely objective data. Nevertheless, the method of evaluation in the two series of cases is similar, so a compari-

TABLE 1.—*Results of Biopsy in Patients with Known or Presumed Pancreatic Malignant Lesion*

Specimen	Total Cases	Results of Biopsy: Positive for Malignancy * Cases	Per Cent	Failed to Reveal Malignancy Cases	Per Cent
Obtained with Vim-Silverman needle	53	36	68	17	32
Wedge-type	56	26	46	30	54

* No false-positive results.

son of the findings would seem to be reasonably sound.

There were 53 patients in the group of 83 who had specimens for biopsy taken with the Vim-Silverman needle whose death was known or presumed to be due to malignant lesion of the pancreas (Table 1). Biopsy revealed evidence of malignant lesions in 68% of the 83 patients and failed to reveal such evidence in 32%. There were 56 patients in whom wedge-type specimens for biopsy were taken who were known or presumed to have died of malignant disease of the pancreas. Neoplasms were seen on biopsy in only 46% of the 56 patients and were not found in 54%. In no case in either group was a false-positive diagnosis of malignant disease made as a result of biopsy.

Consideration of the biopsies which did not reveal malignant lesions (Table 2) shows that approximately a third (36%) of both groups of patients, that is, those from whom wedge-type specimens were taken and those from whom specimens were obtained with the Vim-Silverman needle, presumably had malignant lesions.

TABLE 2.—*Outcome of Patients in Whom Pancreatic Biopsy Did Not Reveal Malignant Lesion*

Specimen	Total Cases	Patients Lived More Than 3 Years No.	Per Cent	Patients Later Known or Presumed to Have Malignant Lesion No.	Per Cent
Obtained with Vim-Silverman needle	47	30	64	17	36
Wedge-type	84	54	64	30	36

Comment

Many surgeons do not utilize biopsy of the pancreas because they consider it hazardous, unnecessary, or unreliable. Complications which have resulted from removal of specimens from the pancreas with the Vim-Silverman needle have been minimal. Occasionally bleeding was encountered at the site of removal, but in every patient this was controlled so that no known bleeding occurred postoperatively. In almost all patients in whom bleeding did occur it was controlled by simple digital pressure. In a few cases a small piece of absorbable gelatin sponge (Gelfoam) was inserted into the site of removal and in several cases a suture was placed in the pancreas. In no patient was drainage of pancreatic juice noted at the time the specimen was taken. Pancreatic juice drained postoperatively from only one patient in the entire group of 99. This drainage subsided without difficulty with appropriate treatment; however, the patient's dismissal from the hospital was delayed until the 21st day after operation. When seen three years later, the patient was in excellent health.* An intraperitoneal abscess developed in one patient after cholecystectomy, exploratory choledochostomy, drainage of the common duct with a T-tube, and biopsy of the head of the pancreas. There was no evidence of pancreatic drainage at any time, and when the abscess was drained nothing was found to incriminate the pancreas.

It is true that an experienced surgeon can diagnose with a rather high degree of accuracy by gross examination the true nature of a mass in the pancreas. This is not true of those who encounter lesions of this type only infrequently. Even the surgeon who is experienced in the field may at times be

* Recently we have seen one other patient in whom leakage of pancreatic juice occurred after biopsy with the Vim-Silverman needle.

in error in his diagnosis. We hesitate to subject a patient who has a mass in the head of the pancreas to the risk of a Whipple-type operation unless a positive diagnosis of malignancy is obtained. In an occasional case a Whipple operation would be considered advisable whether or not the lesion is malignant, but this is an infrequent occurrence, especially with some of the more recently developed operations for drainage of the pancreas in cases of chronic relapsing pancreatitis. Before the head of the pancreas is resected for a relatively small mass, it is quite reassuring, in our opinion, to know, as a result of biopsy, rather than to surmise, that the lesion may be malignant.

It must be clearly realized that biopsy of a pancreatic mass which shows only some degree of pancreatitis by no means excludes the possible presence of neoplasm. Low-grade inflammatory changes usually occur around a pancreatic neoplasm so that such a finding may indicate that a specimen from the growth itself has not been obtained. Multiple specimens for biopsy may be obtained with the Vim-Silverman needle, and, in fact, if initial biopsy does not reveal a malignant lesion in a case in which the surgeon strongly suspects the presence of neoplasm, additional specimens may be taken from a somewhat different region and may reveal such a growth. If a neoplasm is not found by biopsy of the pancreas, the chance of such a lesion being present is the same whether needle biopsy or biopsy of a wedge-type specimen was performed. The accuracy of diagnosis made on study of frozen sections as compared with fixed permanent sections is well established by the present study. It is apparent from this study that the chance of demonstrating a malignant lesion in the pancreas is definitely greater when a Vim-Silverman needle is used than when a wedge-type specimen is taken.

Summary

The results of biopsy of specimens of the pancreas obtained by the Vim-Silverman needle from 83 patients, each of whom had a mass in the pancreas but no obvious evidence elsewhere within the abdomen as to the nature of the mass, were studied. Rapid-frozen sections were made of all specimens and a sufficient amount of material remained for fixed sections on most of them. The condition of all patients was followed for at least three years after operation. The study revealed that the histologic diagnosis made on study of the rapid-frozen section was confirmed in each instance in which fixed sections were available. It was found that of 53 patients who were known or presumed to have died of pancreatic malignant lesions, the malignant lesion was detected on study of the specimen by frozen-section technique in 36% or 68%.

A similar study was made in 110 patients in whom a wedge-type specimen was taken from the pancreas for biopsy. In 56 of the 110 patients who were known or presumed to have died of pancreatic malignancy, study of the specimens revealed the presence of a malignant lesion in only 26, or 46%. Of the patients in whom biopsy of the pancreas did not reveal malignant lesions, an almost equal number (36%) were known or presumed to have died of pancreatic malignant lesions, whether the specimen for biopsy was taken by the wedge or needle method. Complications after removal of a pancreatic specimen by means of the Vim-Silverman needle seldom developed or were inconsequential.

Mayo Clinic.

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Intestinal Recirculation as an Aid to Absorption

An Experimental Study

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The role of surgery in the malabsorption syndrome is directed toward the removal of any contributing gastrointestinal pathology. Intrinsic and extrinsic obstructive lesions are eliminated; intestinal fistulae and short-circuiting operations are frequently taken down to permit the use of the absorptive surface of the entire bowel. Experimental surgical attempts to control excessive caloric loss through hypermotility include vagotomy [1,2,4,5] and use of a reversed segment of the intestine.[8,9] After an extensive small bowel resection, the remaining absorptive mucosa is put to task to maintain nutrition. There is inadequate absorption of foodstuffs, vitamins, and minerals. The possibility of reutilizing the remaining absorptive mucosa by means of recirculation of the intestinal chyme appears to be worthy of study.

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Method

Ten dogs were studied. Each was anesthetized with pentobarbital, 27 mg. per kilogram. Initially, recirculation loops were established in two animals (Fig. 1, *a*). A jejunal circuit was made end-to-side in one and an ileal circuit in the other (Fig. 1, *b*).

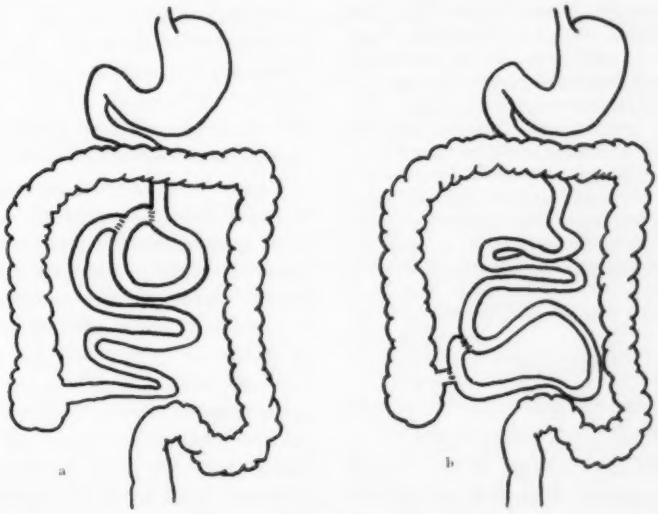

Figure 1

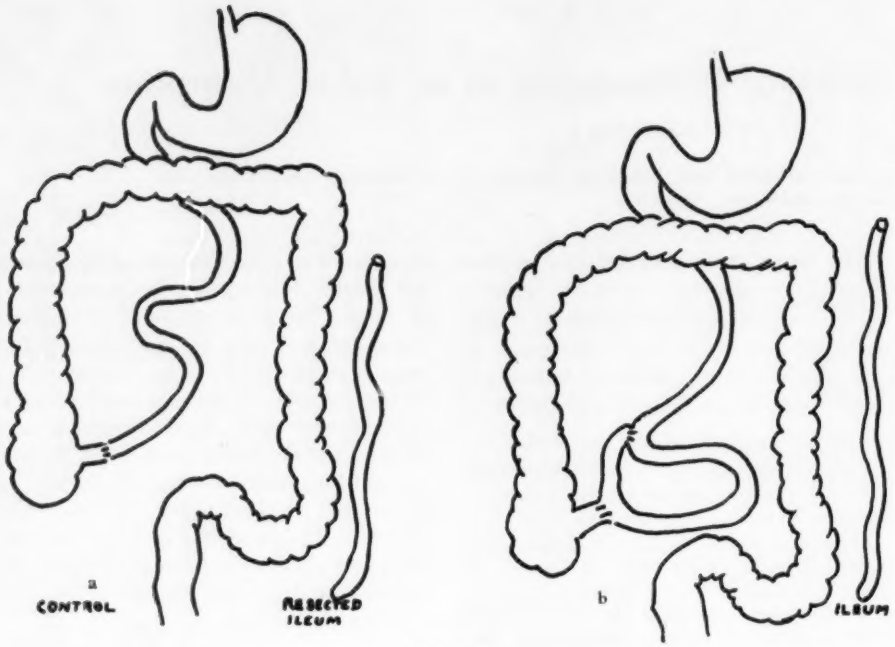

Figure 2

Both animals were reexplored in one week to observe for adverse effects. None were found. Later, these two dogs and eight others underwent a 50% small bowel resection, including most of the ileum. Five had the recirculation procedure on the remaining jejunum (Fig. 2, *b*), while five had end-to-end anastomosis to serve as controls (Fig. 2, *a*). Later the surviving animals underwent the reverse procedure by the taking down of the recirculating loop in the experimental dogs and creating a recirculating loop in the controls. Thus, each animal served as its own control. Postoperative care included parenteral fluids, parenteral vitamins, and antibiotics. Upper gastrointestinal x-ray studies were made. I^{131}-tagged protein and fat uptake observations were done on four of the dogs before and at one- and three-month intervals after surgery. On two dogs such studies were done before and after initial surgery, and again before and after reversal of their original operation.

Results

The two animals with small bowel, intestinal, recirculation circuits maintained or gained weight if no small bowel was resected. When these dogs were reexplored, no evidence of intussusception, dilatation, or obstruction was found in the gastrointestinal tract. However, when these animals and others were subjected to resection of the entire ileum, all lost weight, and had frequent, loose stools. Control animals lost a similar amount of weight after a comparable resection of ileum.

Absorption studies on four dogs with use of I^{131}-tagged protein and triolein showed no significant difference between controls and recirculation dogs.

Fluoroscopic studies demonstrated considerable recirculation of the barium in the small intestinal circuit and no antiperistaltic reflux into the end-to-side jejunojejunostomy. A small amount of barium appeared to remain in the small intestine in excess of two hours.

A single animal died approximately 24 hours after surgery, and was found on autopsy to have pneumonia. A second animal with a 50% resection and a recirculation loop died after 26 days of extreme inanition from diarrhea.

Comment

Survival after extensive small bowel resection in adults attests to the fact that nutrition can be satisfactorily maintained if adequate colon is also functioning. Clatworthy, Saleeby, and Lovingood [3] demonstrated in puppies that 40% to 80% of small bowel could be resected without impairment of growth and development. The few reports of such massive resections in infants again suggest that growth and development will be normal if the small bowel resection does not exceed 50% to 60%.[6]

The studies of adaptation to extensive resection of the small bowel have been summarized by Hartman, Donnell, and Mooney [7]: 1. There is a loss of weight which results in diminished caloric and protein requirement. 2. Microscopic studies in animals show an increase in absorptive area up to 400% in the remaining small bowel. 3. Positive nitrogen balance is reached. 4. Glucose tolerance curves indicate normal glucose absorption. 5. Fat absorption is greatly impaired, with up to 75% of ingested fat appearing in the stools and corresponding reductions demonstrated in oral vitamin A tolerance tests. 6. Animal experimentation shows that the distal small bowel plays a much more important role in fat absorption than the proximal part. 7. The circulating blood volume may be reduced by one-third. 8. Serum calcium may be reduced.

This preliminary report suggests that recirculation of the small bowel chyme has no adverse mechanical or nutritional effect. Indeed, the only animals that maintained or gained weight in the canine colony were the two dogs in which recirculation was performed without resection of ileum. The resected animals in this series of short-term experiments lost much weight. However, after the initial loss, the surviving dogs have maintained weight at approximately one-half to two-thirds of their preoperative weight. Even animals in the dog colony who were operated upon for other purposes, i. e., aortic graft, lost comparable amounts of weight. In regard to this morbidity, Clatworthy [3] observed that confinement of dogs to single cages with the problem of lack of exercise, cross infection, and difficult sanitation with diarrhea was not desirable. Puppies fared better when given the freedom of a farm after extensive small bowel resections.

Summary and Conclusions

Intestinal recirculation appears to be tolerated in dogs.

Some of the intestinal chyme does recirculate after this type of operation.

No immediate nutritional advantage is observed in the animals with ileal resection and intestinal recirculation over the animals with ileal resection and end-to-end anastomosis of the small bowel.

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Bluish Discoloration of the Umbilicus

A Physical Sign for the Detection in a Child of Intra-Abdominal Hemorrhage Following Trauma

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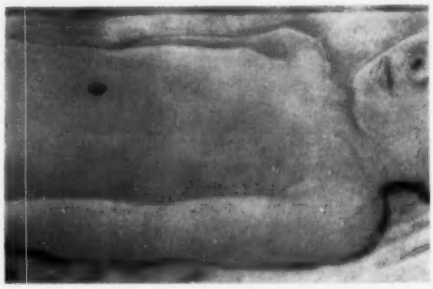
Discoloration of the umbilicus and the umbilical area may be due to coloring agents within the abdominal cavity or to such agents in the umbilical area of the abdominal wall. The importance of such discoloration lies in its diagnostic value; the significant, theoretical consideration of such discoloration is its mechanism of production.

In the following case, the discoloration supported the clinical impression of intra-abdominal hemorrhage, and was due to the direct transmission of the color of free intra-abdominal blood through a thin umbilicus.



Discoloration of the umbilicus which occurred with intra-abdominal hemorrhage following an automobile injury. In the patient, the darkened umbilicus was a pale but definite blue. With the acute anemia resulting from the bleeding, the paleness of the abdominal wall made the discoloration of the umbilicus more prominent.

Report of Case

Chief Complaint.—Abdominal pain following automobile accident.

Present Illness.—This 7-year-old white boy was struck by an automobile about 4 p. m. on March 16. Apparently, the auto struck the boy's right anterolateral chest wall as he was walking across a street. He was temporarily dazed but was not unconscious. He did not vomit. He was taken immediately to the emergency room of University Hospital.

Physical Examination.—The patient appeared to be a fairly well developed, fairly well nourished, 7-year-old, conscious white boy. When first seen, he presented the picture of a patient with multiple contusions. By 7:45 p. m., however, he appeared to be acutely ill, was pale, and was complaining of generalized abdominal pain. The temperature was 99.6 F; pulse rate, 110; respiratory rate, 28; blood pressure, 80/60. There was subcutaneous hemorrhage in the area of the left orbit. Breath sounds over the lung fields were slightly decreased, and there was crepitation of the lateral, lower, right chest wall. There was a definite bluish discoloration of the umbilicus as indicated in the Figure, but there was no evidence of trauma to this area. The abdomen, which was slightly distended, was moderately rigid, with generalized tenderness and rebound tenderness. Peristaltic sounds were hypoactive. Rectal examination was not remarkable. The remainder of the general surgical examination was essentially negative.

Laboratory Data.—Urinalysis was as follows: specific gravity, 1.030; appearance, yellow; albumin, 50 mg. %; sugar, 0; pH, 6.0; and, microscopic examination, 25 leukocytes and 30 to 40 erythrocytes per high power field. Blood cell count: erythrocytes, 3,580,000 per cubic millimeter; hemoglobin, 10.0 gm. %; leukocytes, 24,500 with 57% nonsegmented neutrophils, 29% segmented neutrophils, 13% lymphocytes, and 1% monocytes. Serum amylase: 29 Somogyi units.

Hospital Course.—In view of the clinical picture of acute, internal blood loss and of the bluish discoloration of the umbilicus, the patient was scheduled immediately for exploratory laparotomy. En route to the operating room, no gross abnormalities were noted on an emergency excretory urogram; chest films indicated a fractured right sixth rib, and a small right pneumothorax.

At laparotomy, through a right superior paramedian incision, the umbilicus was found to be thin, and the bluish discoloration of it was due to about 500 cc. of free blood in the intra-abdominal

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cavity. This blood had come from a 2 to 4 cm. deep, 4 cm. long, jagged laceration on the right, anterior, superior surface of the liver. The laceration was so superior that it could hardly be seen but could be palpated. At the time of exploration, bleeding had ceased. The liver laceration was packed with a number of pieces of absorbable gelatin sponge (Gelfoam). A drain was placed through a stab wound to the right of the abdominal incision, which was closed in layers with silk. Immediately before, during, and after the operation, the patient was given 1,000 cc. of whole blood, 1,000 cc. of dextran, and 1,000 cc. of 5% of dextrose in water intravenously. The estimated total blood loss was 1,000 cc.

Postoperative Course.—Postoperatively, the patient's course was one of slow steady improvement. During the first postoperative week, the Penrose drain was gradually removed; the Levin gastric tube was taken out; and penicillin and streptomycin were given intramuscularly. Serosanguineous fluid had to be removed several times by aspiration from the right pleural space with as much as 350 cc. of fluid being aspirated on one occasion. In view of the liver laceration, ambulation was delayed until the first week after laparotomy. The patient was discharged on April 13, the 28th hospital day.

Final Diagnoses.—1. Laceration of liver with hemoperitoneum. 2. Fracture of right sixth rib with pneumohemothorax. 3. Multiple contusions.

Comment

Discoloration of the umbilical area is seen infrequently. Eastman [7] stated that only twice had he seen Cullen's sign in his personal experience, and he pointed out that in both instances the umbilical discoloration was too faint to be recorded photographically.

In the literature, discoloration of the umbilicus and of the umbilical area has been described in association with a ruptured common bile duct, a ruptured tubal pregnancy, a bleeding ulcerated adenocarcinoma of the liver, acute pancreatitis, rupture of the uterus, uterine tumor, ruptured broad ligament hematoma, abdominal aortic aneurysm, carcinoma of the colon, and rectus muscle hemorrhage.[1-16]

In 1906, Ransohoff [13] observed jaundice of the umbilicus in a 53-year-old man with a ruptured common bile duct and bile peritonitis. In his patient, who had been sick several days, on inspection of the abdomen there was noted a marked jaundice of the umbilicus. The navel was a distinct, saffron-yellow color in strong contrast with the remainder of the normal-colored abdomen. This saffron-yellow color was the only evidence of jaundice. At operation, rupture of the common bile duct was found, and the intra-abdominal cavity contained a large quantity of free bile. The abdominal wall was especially thin at the umbilicus, and the absorption of bile was clearly seen at this point. Ransohoff pointed out "it is possible, of course, that by reason of the anatomic relations of the round ligament of the liver to the transverse fissure there is a retrograde flow of bile through the lymphatics toward the navel."

In 1909, Hofstätter [10] described bluing of an umbilical hernia associated with hemoperitoneum secondary to a ruptured tubal pregnancy. This was not true discoloration of the skin, but merely transmission of the color of the free intra-abdominal blood through an extremely thinned-out herniation of the umbilicus.

In 1918, 1919, and 1922, Cullen [4-6] discussed a case of ruptured extrauterine pregnancy in which discoloration of the umbilical area was described. Such discoloration has become known as Cullen's sign. His patient, a woman, 38 years of age, suddenly developed abdominal pain and distention. About one week after the onset of the right, lower, quadrant pain and intermittent attacks of abdominal distention, the umbilical region became bluish-black. When the patient was first seen by Cullen three to four weeks after the onset of the right, lower, quadrant pain, the umbilicus itself was of a greenish blue; above it, there was a faint bluish tinge; below it, the bluish appearance was more intense. The bluish discoloration gradually diminished in intensity during the patient's sojourn in the hospital. At laparotomy, which was performed four weeks after the onset of the right, lower, quadrant pain, a right-sided extrauterine pregnancy and about 1½ qt. of free blood in the intra-abdominal cavity were found. Cullen

concluded that such discoloration of the umbilical area shall be naturally expected "only when there is free blood in the abdomen and shall probably be more likely encountered in thin individuals."

In 1922, Novak [12] reported two cases of ruptured extrauterine pregnancy in which there was discoloration of the umbilicus. He pointed out that "the explanation of this discoloration of the umbilicus in cases of extensive intra-abdominal hemorrhage is probably to be sought in the lymphatics of the umbilical region."

In 1922, Sternberg [15] reported the presence of a bluish discolored umbilicus in a man with hemoperitoneum due to bleeding from an ulcerated adenocarcinoma of the liver. The umbilicus was prominent; below it and surrounding it in a half moon there was evident a bluish-black area on a level with the rest of the skin and containing yellow and green spots. One day prior to the patient's death, 7,000 cc. of serosanguineous fluid was removed by paracentesis.

In 1920, in describing bluish discoloration of the umbilical area in acute pancreatitis, Turner [16] referred to the possibility of pancreatic effusions arriving at this area via the round ligament of the liver.

In 1937, Fallis [8] described two cases of acute pancreatitis with yellowish discoloration about the umbilicus but without a blood-stained peritoneal exudate. He proposed that, with the retroperitoneal position of the pancreas, effusions of blood resulting from the disintegration of the gland could travel around in the subperitoneal space and, reaching the midline anteriorly, could pool in the potential subumbilical space.

In 1945, Cox [2] described discoloration of the abdominal wall in acute pancreatitis in a 65-year-old woman. On the third day of the disease, a discolored area appeared on the skin around the umbilicus; on the seventh day, a similar but smaller area was first noticed in the left flank. These areas, lacking uniformity in color and showing an admixture of distinct blue, green, and yellow elements, resembled exactly the color changes in a fading ecchymosis. A localized mass developed in the left hypochondrium, and contained 3 oz. of blood when it was drained. Cox stated that the flank discoloration was due to extraperitoneal spread of blood and pancreatic secretion. He added that, in those cases in which an umbilical fascia does not constitute a complete covering for the umbilical ring, such spread of blood and pancreatic secretion may continue from the extraperitoneal and subcutaneous tissue into the umbilical area.

In 1949, Fallon and Manning [9] emphasized that the Hofstätter-Cullen sign need not be blue, that it can appear elsewhere than at the umbilicus, that it is far from pathognomonic of extrauterine pregnancy, and that, probably, it can be caused by any condition producing colored intra-abdominal fluid. According to them, the location of the discoloration of the abdominal wall in one case of theirs and in two somewhat similar cases in the literature of ectopic pregnancy, as well as the more ordinary localization over hernias, in scars, and at the umbilicus, suggested that the pigments that usually produce the phenomenon may reach their destination by following ordinary fascial planes and openings rather than by depending upon exceptional lymphatic function or subvisible peritoneal apertures.

In 1958, Cadman [1] reported that the commonest causes of Cullen's sign in order of frequency are ruptured tubal pregnancy, rectus muscle hemorrhage, acute hemorrhagic pancreatitis, and rupture of the uterus, and added three further examples of the sign, the associated conditions being a ruptured abdominal aortic aneurysm, carcinoma of the colon, and a uterine tumor. Cadman pointed out that this sign is primarily an indication of the presence of blood or blood-stained fluid in the abdominal wall. He emphasized that the blood may arise retroperitoneally (most frequently from the Fallopian tubes, pancreas, or uterus) and spread in the extraperitoneal tissues to the subcutaneous tissue at the umbilicus. Alternatively, he added, the blood may arise within the abdominal wall itself, usually from a rupture of the rectus muscle.

In 1958, Scott, Novak, and Tindale [14] pointed out that the blue-black discoloration of the umbilicus in association with an incarcerated umbilical hernia and underlying blood from a ruptured ectopic pregnancy, such as that described by Hofstätter in 1909, is not to be considered a true Cullen's sign. They picture and report what they considered to be a true Cullen's sign. It developed post partum and secondary to a large broad-ligament hematoma. They implied that the true Cullen's sign is the result of the retrograde lymphatic spread of blood pigments from the pelvis to the umbilical region.

In 1958, Merrill [11] stated that Cullen's sign consists of ecchymotic discoloration of the periumbilical skin and subcutaneous tissues. In a full-thickness biopsy of the anterior abdominal wall in the region of discoloration of a 43-year-old Negro woman with a right, ectopic, tubal pregnancy with tubal abortion, the significant microscopic findings were a diffuse extravasation of intact blood and small amounts of hemosiderin pigment. Merrill concluded that the presence of abnormal apertures or breaks in the continuity of the peritoneum permit blood from the peritoneal cavity to reach and to remain in the abdominal wall.

The bluish discoloration of the umbilicus observed in the case reported in this paper is not considered to be a typical example of Cullen's sign for two reasons: first, this discoloration did not develop in a woman with a ruptured tubal pregnancy but developed in a 7-year-old boy who had been struck by an automobile, and, second, the discoloration did not appear one week after the onset of acute hemorrhage but appeared within an hour or two after an accident.

The bluish discoloration in this boy is similar to that observed in the case of Hofstätter.[10] In his patient, the color of the blood from a ruptured tubal pregnancy could be seen through the thinned-out umbilicus of an incarcerated umbilical hernia. In the case reported in this paper, the color of free intra-abdominal blood was visible through the thin umbilicus but not through the thicker adjacent abdominal wall where there were muscles and more abundant subcutaneous fat; and no deposits of blood or breakdown products of blood were demonstrated in the umbilicus or the abdominal wall.

Summary and Conclusions

After trauma to the chest or abdomen of a child, the possibility of intra-abdominal hemorrhage should be suspected with the rapid development of a bluish discoloration of the umbilicus.

A case of a 7-year-old white boy in which such bluish discoloration occurred is reported. In this case, the visible bluish discoloration was due to the direct transmission of the color of free intra-abdominal blood through a thin umbilicus. No deposits of blood nor breakdown products of blood were demonstrated in the umbilicus or the abdominal wall.

Various proposed mechanisms for the production of umbilical area discoloration are reviewed.

327 E. State St.

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Acute Noncalcareous Cholecystitis with Associated Mesenteric Adenitis in a Child

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Cholecystitis in children is an uncommon disease. Less than 400 proved cases have been reported in the literature.[1] The following case report is of interest, in that acute noncalcareous cholecystitis in a 9-year-old girl was associated with a mesenteric adenitis.

Report of Case

On July 17, 1957, the patient was admitted to Mercy Hospital with the diagnosis of acute abdomen, most likely appendicitis. Laboratory and physical findings revealed a white blood count of 12,500, and a differential count as follows: lymphocytes 26; monocytes 2; polymorphonuclears 72; hemoglobin 13.0 gm., 82%. Urinalysis was negative except for acetone, which was 3+. The temperature was 102 F rectally. There was exquisite tenderness throughout the whole right abdomen with rebound and rigidity to palpation.

Under general anesthesia a right lower quadrant muscle-splitting incision was made, and the peritoneal cavity entered. The appendix was found to be normal. There were multiple mesenteric nodes, and the diagnosis of acute mesenteric adenitis was entertained. However, because of the severity of the symptoms, the gallbladder was explored and found to be acutely inflamed, and extremely tense. Consequently, a right upper abdominal quadrant paramedian muscle-retracting incision was made. The acutely inflamed gallbladder was removed and the gallbladder bed drained through a stab wound. The postoperative course was uneventful, and the patient was discharged on the fifth postoperative day. Culture from the cystic duct revealed no growth in 48 hours.

The pathological report was as follows: Representative sections from the wall of the gallbladder are marked by diffuse and prominent infiltration of polymorphonuclear leukocytes, necrosis, and edema. The deposition of the pink-staining, protein-like material (edema) results in a marked thickening of the bladder wall, especially in the serosal and muscular layers. The necrotic and hemorrhagic changes are diffuse throughout, although the mucosal layer is not appreciably involved. These alterations are seen prominently in areas of vascular dilatation and thrombus formation, necrosis being consistent with coagulative type. The thrombi impart a red, amorphous appearance, with no apparent evidence of organization. Similarly, no bacterial colonies are identified. Other than moderate degenerative changes and scanty focal areas of necrosis, the mucosa is conspicuously free of inflammatory changes. Within the appendiceal submucosa are prominent lymph follicles exhibiting germinal centers. Despite the presence of an Enterobius vermicularis organism within the lumen, inflammatory or destructive changes in the mucosa, submucosa or muscularis are not conspicuous.

Through 1948, Ulin et al. collected 326 valid cases of cholecystitis in children 15 years of age or younger. Since that time 12 additional cases have been added to the American literature.[2-4] Ulin found 67% had associated cholelithiasis and 6% had choledocholithiasis, and that the disease was frequently associated with acute infections such as typhoid fever, scarlet fever, and measles. Since 15% were misdiagnosed

Fig. 1.—Fresh gallbladder specimen showing acute cholecystitis without evidence of stones.

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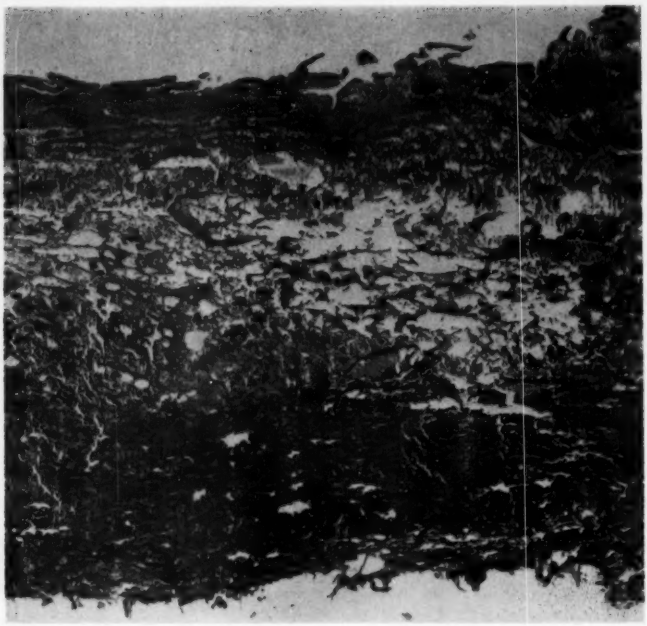

Fig. 2. — Photomicrograph of gallbladder wall showing acute inflammation.

preoperatively as appendicitis, he suggested palpation of the gallbladder when appendiceal pathology was not discovered.

Mesenteric adenitis associated with acute cholecystitis has received only passing attention. In one of the cases reported by Glenn and Hill, enlarged mesenteric nodes associated with enteritis and glomerulonephritis were discovered at a second operation. In another, autopsy revealed gangrenous cholecystitis and hyperplasia of the mesenteric node with peritonitis and typhoid fever.

Summary and Conclusion

The case in this report would indicate that even though pathology in the form of mesenteric adenitis is found when the appendix is normal, the gallbladder should still be palpated for abnormality.

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Hypothermia and Extracorporeal Circulation

Experimental Studies of Profound Hypothermia of 10 to 20 C

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The many advantages of combining low flow extracorporeal circulation and hypothermia for open heart surgery have been stressed by recent reports from this clinic and laboratory.[1-5] These studies were concerned with temperatures of 28 to 30 C combined with extracorporeal flow rates of 25 to 50 cc. per kilogram per minute. To meet other clinical situations that might demand either complete or almost complete circulatory standstill for appreciable periods of time, it would be desirable to use temperatures below 20 C. Since the introduction from this clinic of a feasible method of precise control of the body temperature,[3,6] the clinical application of this degree of hypothermia became possible for the first time. This report outlines the first of our studies in the laboratory on extension of the advantages of hypothermia to these low levels.

Methods

Adult dogs of both sexes were used. Anesthesia was induced by intravenous pentobarbital sodium. The blood oxygenator and pump was a slightly modified DeWall-Lillehei apparatus. Hypothermia was induced, controlled, and corrected by a heat exchanger placed in the extracorporeal circuit as described in an earlier paper.[3] The animals were connected to the pump-oxygenator by the femoral artery and femoral vein and jugular vein. Induced cardiac standstill was obtained by the injection of a solution containing potassium citrate 0.86%, magnesium sulfate (hydrated) 2.46%, and neostigmine 0.001% into the ascending aorta after the distal occlusion of this vessel.

Arterial and venous blood oxygen levels were determined by the method of Hickam and Frayser.[7] The arterial and venous pressures, Lead II of the electrocardiogram, the frontoparietal electroencephalogram were all monitored.

By means of thermistors, the temperature of the mid esophagus, upper rectum, chest wall, and thigh were recorded in many experiments.

A right thoracotomy was carried out in the sixth interspace in all of the animals. Respiration was controlled with a mechanical respirator using room air without oxygen supplement in the first part of these studies, but in the latter part of the studies oxygen was added. In all the animals, tapes for occlusion were placed around both the superior and inferior venae cavae and around the distal part of the ascending aorta. In the study, the dogs were first put on partial by-pass with assisted circulation at perfusion rates of 50 cc. per kilogram per minute. When the temperature reached 30 C in the esophagus, the vena cavae were occluded and the heart put into standstill by coronary injection of the cardioplegic solution. Then on this same flow rate, the animal's esophageal temperature was reduced to below 20 C.

In Group I, the animals were put into complete circulatory arrest by stopping the extracorporeal pump for periods of 10 to 30 minutes. In some, blood samples for determination of arterial and venous oxygen saturations were obtained just before the pump was stopped, immediately after it was restarted, and then at appropriate intervals throughout the remainder of the procedure. The venous samples were removed from the extracorporeal tubing just before the venous blood entered the venous pump. The arterial samples were obtained from the femoral artery. In one dog in each group, distal femoral venous samples were taken in addition to the mixed venous ones.

In Group II animals, the oxygenator was bypassed, but the perfusion was continued at rates of approximately 25 cc. per kilogram per minute. During the oxygenator by-pass, there was no venous blood, of course; so the single samples were obtained which represented the circulating blood.

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TABLE 1.—*Oxygen Saturation Data: Circulatory Standstill, Group I*

Dog	Perf., Min.	Lowest Esoph. Temp.	Standstill, Min.	Oxygen % Saturation Arterial/Venous During Circulatory Standstill			After Rewarm % Sat. Art/Ven.	Result
				1 Min. Before	1 Min. After	4 Min. After		
3	29	20 C	10					Survived
1	111	22 C	11					Survived
4	30	18.5 C	11					Survived
6	32	19 C	15	99/72.9	100/30		100/40	Survived
8	35	18 C	16	100/53.8	130/30	100/64	100/62	Survived
25	32	11 C	20	100/90	100/90.6	100/62	100/76	Survived
2	66	18 C	11					Died
5	51	17.5 C	15	98/75	100/28		100/28.9	Died
7	60	20 C	15	100/97.3	100/69.6	100/58.1		Died
19	93	10.5 C	30	100/98.8	100/97.4	100/85	100/34	Died
24	84	13.2 C	21	100/90.5	100/78	100/75	100/59	Died
26	45	10 C	21	100/95	100/86	100/83	99/66	Died

For rewarming in both Group I and Group II animals, the pump-oxygenator was again put back into the system, the flow rate increased to 50 cc. per kilogram per minute, and then the temperature increased to 30 C in the esophagus as rapidly as possible. At the temperature of 30 C, the aorta was opened and the coronary perfusion was resumed. When a temperature of 35 to 37 C was reached, the animal was taken off the pump-oxygenator and his blood volume was readjusted to approximately normal. After this was done, the animal's chest was closed, and the survivors were followed for at least one week.

Results

In Group I, 12 dogs were studied (Tables 1 and 2). There were six who survived these experiments, while six died within the first eight postoperative hours. One died because of irreversible ventricular fibrillation, and in this animal there occurred a technical accident with the perfusion that explains this event. In another dog, on rewarming the venous oxygen saturation was only 28%, owing to inadequate perfusion. This animal did not survive. Three of the animals died from pooling of the blood in the portal circulation, showing at autopsy extensive hemorrhagic areas in the bowel and marked edema of the liver. The sixth dog had pulmonary edema and succumbed nine hours after closure of the chest. It will be noted that the esophageal temperatures in this group were generally higher than those in Group II.

The levels of oxygen in the arterial and venous blood from Group I are shown in Table 1. In all experiments except Dog 8, the oxygen saturation of the venous blood during perfusion but before circulatory arrest was above 70% in spite of low flow rates. Two of the dogs had venous saturations of oxygen above 95% with temperatures during perfusion of 20 C and 10.5 C

TABLE 2.—*Perfusion Data, Group I*

Dog	Lowest Esoph. Temp.	Time Cardiac Standstill, Min.	Cooling Time, Min.	Time Circulation Arrest, Min.	Rewarming Time, Min.	Total Time, Min.
3	20 C	30	11	10	18	39
1	22 C	63	33	11	78	122
4	18.5 C	28	8	11	22	41
6	19 C	27	8	15	24	47
8	18 C	40	11	16	25	51
2	18 C	22	13	11	53	77
5	18 C	27	10	15	41	66
7	20.5 C	24	8	15	52	75
19	20 C	80	36	30	57	123
24	10.5 C	70	35	21	49	105
25	11 C	37	12	20	20	52
26	10 C	48	17	21	28	66

TABLE 3.—*Oxygen Saturation Data, Oxygenator By-Pass, Group II*

Dog	Perf., Min.	Lowest Esoph. Temp.	Time Oxygenator By-Pass, Min.	Control % Sat. Art/Ven.	20 C % Sat. Art/Ven.	% Saturation Mixed Blood (Art. & Ven.) Minutes After Oxygenator Off 5	10	15	20	25	Rewarm % Sat. Art/Ven.	Result
9	50	18 C	15	95.6/74.3	100/86	95.4	88	74			100/75	Survived
20	65	13 C	20	87.3/37.5	99/94.5		90		74.4		99/70	Survived
11	58	16 C	25	86/30	96/90		97.7			64.9	99.3/47.2	Survived
13	49	14 C	25	100/73.8	100/89.3					54	94/78.8	Survived
17	54	13 C	25	85.5/45.1	100/63.8		35			30	100/31.3	Survived
14	78	18 C	25	92.1/76	100/90		75.5		60.0		99/69.5	Survived
10	65	13 C	20	94.8/32.5	97/81						100/38	Survived
23	77	8.5 C	21		100/87.6		88.4		76.1		99/82	Survived
15	70	18 C	25	94/80.4	100/95.5		90.1		77.1	66.7	99/65	Died
18	42	15 C	25	94/38	100/50		65.3				97.7/24.1	Died
12	65	13.5 C	30	100/58	100/93.8		72.8		43	36.5	98/43	Died

TABLE 4.—*Perfusion Data, Group II*

Dog	Lowest Esoph. Temp.	Time Cardiac Standstill, Min.	Time Cooling, Min.	Time Oxygenator By-Pass, Min.	Rewarming Time, Min.	Total Perfusion Time, Min.
9	18 C	33	10	15	25	50
10	16 C	46	14	20	27	61
20	13 C	50	15	20	48	65
11	16.5 C	50	14	25	19	58
13	14 C	37	8	25	26	49
17	13 C	49	15	25	17	54
14	12 C	61	24	25	20	77
15	18 C	57	11	25	31	70
18	15 C	36	8	25	9	42
12	13.5 C	57	21	30	24	65
23	8.5 C	59	21	20	36	77

TABLE 5.—*Mean Systemic Blood Pressure in Mm/Hg During Perfusion, Group I*

Dog No.	Control	Beginning of Cooling	At 20 C	Just Before Arrest	Arrest	Beginning of Rewarming	At 30 C	End of Rewarming
1	115	90	55	55	0	35	100	105
2 *	125	90	70	70	0	80	70	120
3	115	85	90	90	0	55	75	80
4	110	40	55	55	0	20	80	70
5 *	100	80	50	50	0	50	70	65
6	110	70	65	65	0	60	85	80
7 *	85	70	45	45	0	40	80	50
8	100	120	95	95	0	40	110	85
19 *	90	55	40	30	0	50	55	65
24 *	100	80	50	40	0	40	40	70
25	110	80		55	0	25	70	80
26 *	95	90	60	45	0	35	50	95

* Died.

TABLE 6.—*Mean Systemic Blood Pressure in Mm/Hg During Perfusion, Group II*

Dog No.	Control	Beginning of Cooling	At 20 C	Just Before By-Pass	During By-Pass	Beginning Rewarming	At 30 C	End of Rewarming
9	105	65	45	45	35	50	80	95
10	120	100	105	80	75	100	75	65
11	100	75	55	55	45	65	70	55
12 *	110	60	45	45	35	50	75	60
13	110	85	80	80	40	55	90	75
14	100	80	55	50	30	40	45	45
15 *	105	115	90	70	60	55	55	65
17	120	50	30	30	25	45	45	55
18 *	110	55	50	50	30	35	55	45
20	70	55	50	50	40	50	75	75
23	110	60	50	50	40	35	85	45

* Died.

respectively. After by-pass of 10 to 20 minutes where there was complete circulatory standstill, decrease in oxygen was noted in the venous blood, though in some instances this was not marked.

In Group II there were 8 survivors in 11 experimental subjects (Tables 3 and 4). The oxygen levels in the venous blood are shown in Table 3. During the oxygenator by-pass, there was a gradual drop in the oxygen saturation in all instances. The three deaths were due to pooling of blood in the portal system.

The blood pressure variations from Group I and Group II are shown in Tables 5 and 6 respectively. Temperature gradients for both groups are shown in Table 7.

The differences in Group I and Group II are not striking. In Group I ventricular fibrillation occurred in three dogs. This was a higher incidence than experienced in other experiments in this laboratory.[2] It will be noted that in some instances in both groups the venous oxygen levels were quite low before either hypothermia or perfusion was started. This was due to poor pulmonary ventilation. In the last half of the study this was corrected. There was, however, a higher mortality rate in Group I, where all circulation was stopped, than in Group II.

Figure 1 illustrates two interesting points. First, it will be noted that there is a marked lag in the temperature fall in the thigh and rectum as compared with the esophagus. The venous oxygen saturations are governed by these temperatures as is so well shown when the mixed venous specimen is compared with the samples taken from the distal femoral vein. There is, in addition to the cooling lag, a similar lag in the rewarming rate. In contrast to the first graph, Figure 2 shows that the mixed and femoral venous

TABLE 7.—*Temperature Gradients in C, Group I*

Dog No.	Beginning of Cooling			Lowest Temperature and Drift During Circulatory Arrest or Oxygenator By-Pass			Rewarming		
	Esoph.	Rect.	Thigh	Esoph.	Rect.	Thigh	Esoph.	Rect.	Thigh
				Group I					
25	30	31.9	29.8	11.5-17.5	22-19	26.5-26.5	34	21	28.2
24	31.2	34.5	33.5	13.2-15.5	17-18	17.5-20	33.5	32	31.5
19	31	36	34.2	10.4-11	19.8-17	22-24	34	32.8	29.5
26	31.2	33.1	31	10-14.2	19.1-19.5	22-23.2	34	33	29
				Group II					
20	31	34	32	13	17	22	35	32	29
22	30	32.8	33.6	8	12	28	36	36	28
23	29	30	29	8.5	16.5	24	35	33.5	25

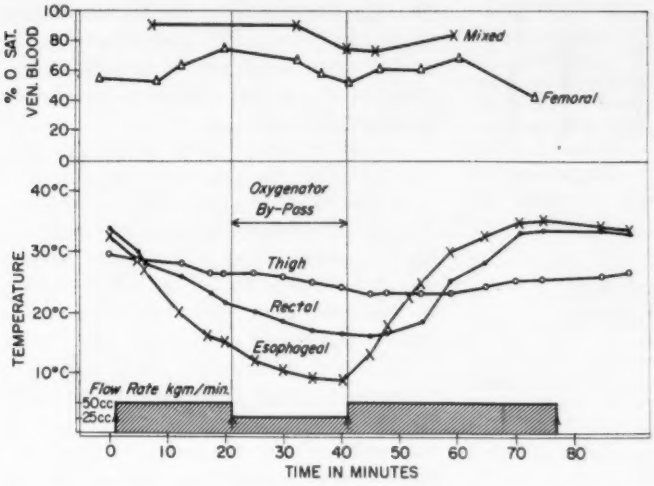

Fig. 1 (Dog 23, Group II).—This graph shows venous oxygen levels from the distal femoral vein and the mixed venous pool obtained at various temperatures in the thigh, rectum, and esophagus. Note the moderate decrease in the oxygen saturation even after 20 minutes of oxygenator by-pass.

oxygen levels remained about the same, for the cooling and rewarming temperatures in this dog remained comparable. Why this particular animal showed this inconsistency in the temperature changes is not known, for this was the exception rather than the rule. This dog is also of unusual interest in that the mixed venous blood just after restarting the circulation after 20 minutes of complete circulatory standstill showed a very high venous oxygen level. This may have been due to both the low temperature and to the uniform cooling rate.

Figure 3 illustrates another experiment where the oxygenator was by-passed, and, even though the esophageal temperature was low, there was a steady fall in the oxygen saturation of the circulating blood during the by-pass. When one looks back on Figure 1, it is quite obvious that this diminution in saturation in the mixed venous blood when the oxygenator is removed from the extracorporeal system might be explained by the leak into the central system of pooled blood from the extremities and other areas of slow circulation.

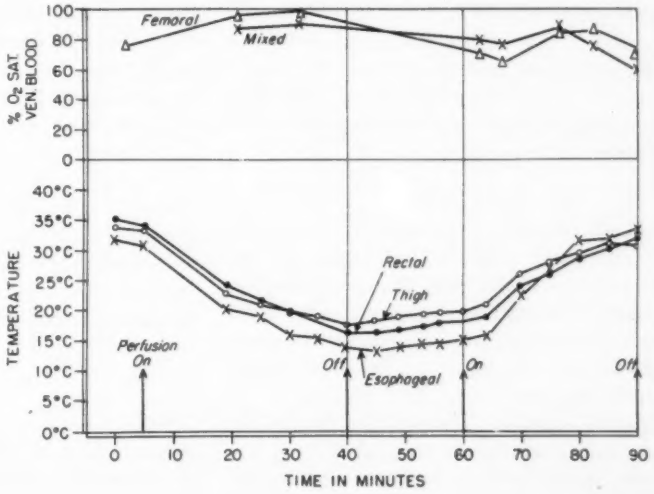

Fig. 2 (Dog 24, Group I).—This graph shows venous oxygen levels from the distal femoral vein and mixed venous pool obtained at the various temperatures in the thigh, rectum, and esophagus. Note the uniform cooling and similar oxygen levels in the two areas of sampling.

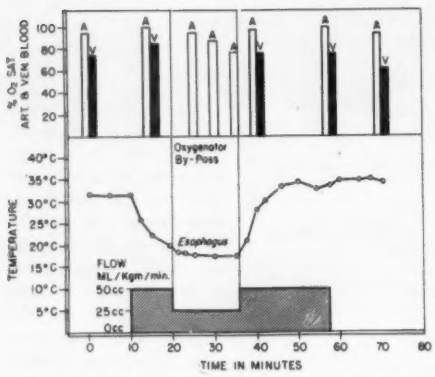

Fig. 3 (Dog 9, Group II).—A graph showing the A-V oxygen difference at various esophageal temperatures. Note the moderate decrease in the oxygen saturation during oxygenator by-pass even though only very low perfusion was used.

It is also of interest to call attention at this time to the efficiency of this method of induced cardiac standstill. It will be noticed that most of the animals were in standstill for well over 30 minutes. With one exception the heart was easily brought back to normal rhythm. In all respects, the animals acted exactly like the ones reported in our previous studies using this technique for induced cardiac standstill. It is interesting to note that in no instance were precautions taken to prevent left heart distention.

The electroencephalogram was monitored constantly, and somewhere between esophageal temperatures of 15 and 20 C all activity ceased in the electroencephalogram and it did not return until these temperatures were passed in the rewarming period. The electroencephalogram then returned to normal during the rewarming time.

Comment

Hypothermia of below 20 C is the only means now available of reducing the metabolism to the point that the circulation can be suspended or drastically reduced for long periods of time. These low temperatures alone, judging from the experimental work of Gollan [8-11] and Niazi and Lewis,[12-15] are not injurious. The principal danger that has to be considered before clinical application, stems from the problem of reversing the hypothermia. This danger no longer exists since the body temperature can be precisely controlled with a heat exchanger made part of an extracorporeal pump oxygenator system.

Central or core cooling performed in a rapid manner by the technique described here may result in uneven cooling and significant differentials in the temperature of various areas. Of most importance in this regard is the brain. From other studies in this laboratory, the brain temperature lags behind the esophageal and rectal temperature, particularly when esophageal temperature of 20 C is reached. The electroencephalogram may be used as an indirect indicator of the temperature since our experimental studies have shown that at esophageal temperatures between 15 and 20 C electrical activity tends to disappear. The uneven temperature gradients may also cause the cold to be "stored" in areas that are slow to rewarm. This can be followed by a drift downward of the body temperature if perfusion is stopped too early.

In the studies, the oxygenator was removed from the system to see if low perfusion rate alone would be adequate. At the temperatures used, the oxygen need can be almost supplied by that in physical solution. The trauma to the blood by the oxygenator therefore could be greatly reduced. Since the brain may not be cooled to the same low level as the esophagus, this small oxygen supply may be needed even at esophageal temperatures of 10-15 C. This could be supplied either by intermittent use of the pump oxygenator, or by perfusion alone.

In other studies [16] performed in this laboratory, temperatures below 10 C have permitted complete circulatory standstill for one hour, followed by survival in all 11 dogs tested. These animals did not have a thoracotomy, and cardioplegia was induced with cold.

Summary

Studies of hypothermia of 10 to 20 C induced and controlled by a heat exchanger are presented. In one group of experiments

the circulation was completely stopped, while in the other perfusion without oxygenation was employed. There is an advantage in continuing a small amount of perfusion even at the low temperature used in these experiments.

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Resection of the Aorta for Malignant Invasion

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Progress in the field of vascular surgery has resulted in reduction of the mortality and morbidity rates associated with local resection of the aorta. Such reduction of the mortality rates in association with any major operation inevitably results in an extended application of that procedure. Thus, local involvement of major blood vessels by neoplastic infiltration should no longer, of itself, deter the surgeon from accomplishing excision of such a lesion. To demonstrate the application of this principle, the following case is presented, in which the abdominal aorta was resected because of involvement by a late recurrence of ovarian carcinoma.

Report of a Case

A 59-year-old married woman was first seen at the Mayo Clinic in August, 1953, complaining chiefly of a tender mass in the right lower abdominal quadrant, first noted two months previously. At examination the only pertinent finding was a mass 8 by 10 cm. arising from the region of the right ovary. The mass was mobile and firm, with apparent cystic areas. The preoperative diagnosis of right ovarian tumor was confirmed at surgical exploration on Aug. 17. Local extension of this tumor to the mesentery of the rectosigmoid had occurred, but no other metastatic processes were detected. The tumor was thoroughly encompassed by the dissection and was excised. The left tube and ovary likewise were removed. Lymph glands removed from the iliac and obturator areas were found to be free of metastatic involvement. The tumor proved to be a Grade 3 (Broders) papillary adenocarcinoma. The convalescence was smooth, and 12 roentgen-ray treatments were administered from Aug. 27 to Sept. 9, making a total of 1,800 r delivered to the pelvic region. The patient returned in March, 1954, for reexamination; no evidence of residual carcinoma was found.

In January, 1958, the patient again returned, complaining once more of a mass in the right side of the abdomen which she had discovered while she was massaging her abdomen to relieve gaseous distention. Examination at this time revealed a firm mass fixed to the posterior abdominal wall at the level of the umbilicus, slightly to the right of the midline. Results of pelvic examination were entirely negative. Recurrent carcinoma was suspected, but at surgical exploration a mass thought to be an aneurysm of the abdominal aorta was encountered. This was located just above the bifurcation of the aorta, involving also a portion of the right common iliac artery. Since permission of the patient for resection of the aorta and insertion of a graft had not been obtained prior to the exploration, resection and grafting could not be carried out at that time.

Reoperation was accepted and was performed on June 21, 1958. Careful exploration revealed no abnormalities other than the single mass previously encountered. Needle biopsy of the mass showed it to be carcinoma of the type previously removed. The lesion was intimately adherent to the lower abdominal aorta and the proximal right common iliac artery, as well as to the right inferior vena cava. An interesting incidental finding was the presence of a left inferior vena cava in this patient. The mass thus appeared to be an isolated recurrence of the ovarian carcinoma removed five years previously. Removal of the recurrent process therefore seemed to offer reasonable hope for complete cure. There was obviously no plane of cleavage between the lesion and the terminal portion of the aorta, the right common iliac artery, or the inferior vena cava. The mass was therefore removed in continuity with the adjoining section of aorta, the right common iliac artery, and a portion of the anterior wall of the inferior vena cava. A Tapp-Edwards crimped nylon bifurcation aortic prosthesis, extending from 2 cm. below the level of the renal vein to 1.5 cm. distal to the aortic bifurcation, was inserted. The right inferior vena cava was reconstructed. Excellent peripheral pulses were elicited after removal of the clamps temporarily occluding the aorta and the iliac arteries. The patient was dismissed on June 30, 1958, after a smooth convalescence.

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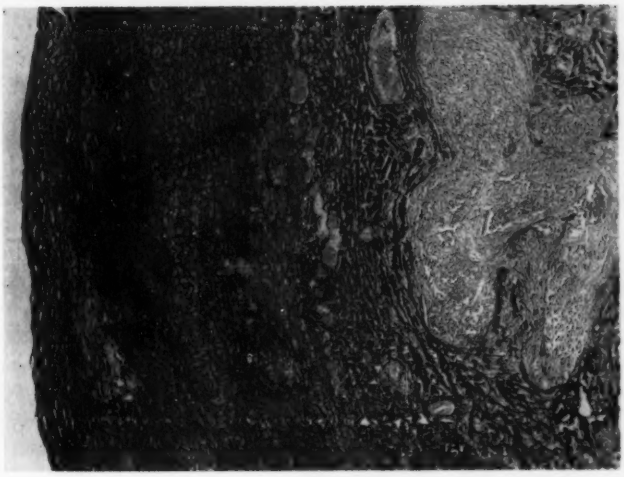

Fig. 1.—Invasion by the tumor of the adventitial layer of the aorta, the lumen of which is to the left. Elastic fibers of the tunica media are distinctly demonstrated by van Gieson's stain (×30).

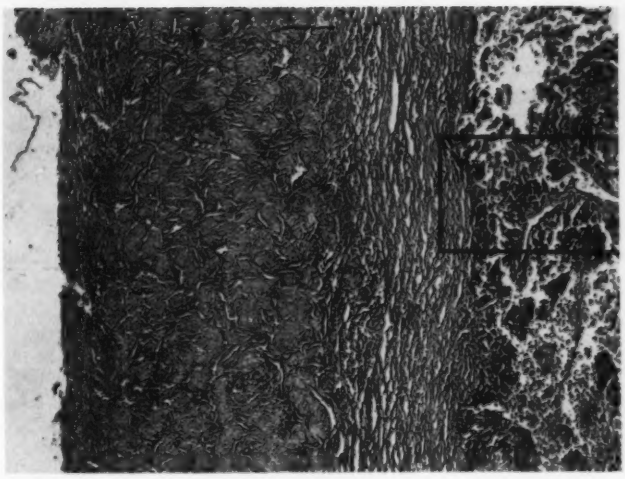

Fig. 2.—The inferior vena cava where the adventitia is also infiltrated by carcinoma (hematoxylin and eosin; ×50).

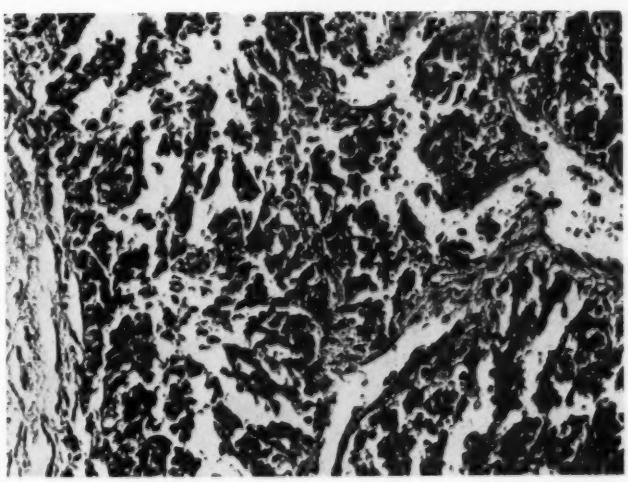

Fig. 3.—Higher magnification of the outlined area shown in Figure 2, to show the cellular detail of the malignant lesion, a detail which is identical with that of the original ovarian tumor removed five years prior to this report (×200).

Supplementary roentgen therapy to the abdomen was administered after dismissal of the patient.

Comment

This case presents several features of interest. In general, carcinoma of the ovary is accompanied by a poor prognosis, the five-year survival rate being from 15.5% to 30.4%.[1] Recurrence usually develops in the form of generalized abdominal carcinomatosis. It is very unusual for such a lesion to recur in the form of a solitary metastatic process, particularly after the long interval of five years. In this case the metastatic lesion seemed well encapsulated. It was inseparably attached to the aorta and the inferior vena cava as a result of carcinomatous infiltration of the adventitial layers of both vessels, as illustrated by the photomicrographs (Figs. 1, 2, and 3). In the absence of other evidence of metastasis five years after the initial excision, there is reason to hope that a cure has been effected.

Of additional interest is the fact that this patient was found to have a left inferior vena cava. Therefore, although reconstruction of the right inferior vena cava was performed, it probably would have proved satisfactory in this case to ligate and excise this vessel. Recently it has been demonstrated that a left inferior vena cava may be a commoner anomaly than was previously appreciated. In a series of 100 dissections three examples of persistent left vena cava were encountered.[2]

Surgery of the aorta to date has been confined chiefly to the treatment of nonmalignant lesions of the aorta itself, such as coarctation, aneurysm, and occlusion. Local involvement of the aorta by a malignant invasive lesion may, in certain selected instances, now warrant aortic resection. Crawford and De Bakey[3] have reported excision of portions of the inferior vena cava and abdominal aorta to accomplish removal of a retroperitoneal sarcoma in two patients. Resection of a portion of the abdominal aorta for a recurrent malignant lesion likewise has been performed by Moore.[4] It must be emphasized that unless the involvement of the aorta by malignant invasion is clearly localized, aortic resection probably is not advisable.

Summary and Conclusion

Resection of the aorta was required to enable complete excision of a malignant tumor infiltrating the abdominal aorta in one patient. The excised terminal portion of the aorta was replaced with a prosthetic graft. The occurrence of local involvement of the aorta by malignant invasion may in certain selected instances warrant aortic resection.

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Removal of Sodium-Copper Chlorophyllin from Solutions by Washed Human Red Blood Cells

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The reasons for obtaining excellent clinical results from the use of the water-soluble derivatives of chlorophyll in the treatment of infected wounds have not been fully determined. A small amount of evidence from the laboratory and a large amount of clinical data attest, however, to the efficacy of the drug in this condition.

Dunham,[11] in studying the influence of chlorophyll on fibroblasts in tissue culture, reported that in all instances the fibroblasts grew more luxuriantly in the cultures containing chlorophyll than in the controls. He concluded that preparations containing proper concentrations of chlorophyll would have similar effects on fibroblasts in wounds which were in the process of healing.

Buergi[7] found that chlorophyll produced faster healing in experimentally produced wounds in guinea pigs and rabbits than any other preparation. The depths of the wounds dried; rich granulation tissue grew promptly; growth of epithelium was found; the wounds became smaller, and healing of the wounds was noted in about 10 days without evidence of inflammation.

Of a number of agents tested, Smith and Livingston[22] determined that only the preparations of chlorophyll showed any statistically significant effect in accelerating the healing of traumatic and thermal wounds. On the basis of these observations, they suggested that preparations of chlorophyll should be used much more extensively in the treatment of burns and wounds.

Smith[21] found that chlorophyll added to tissue cultures of embryonic fibroblasts caused an almost immediate response in growth with elimination of the usual 6-to-18-hour lag period. The stimulation of growth was maintained by replenishing the medium with chlorophyll every 48 hours.

Gruskin[12] treated over 1,200 patients with a wide variety of infections with chlorophyll in a solution, in an ointment, and in a suppository. The results were considered beneficial.

Boehringer[5] noted that an ointment containing chlorophyll produced better granulation tissue than control ointments. Epithelial growth was the same with the chlorophyll and the controls. The favorable effect of chlorophyll in chronic wounds was particularly impressive.

Holmes and Mueller[13] reported that the time of reaction to irradiation was shortened and healing accelerated when the lesion was treated with an ointment containing chlorophyll. Infection was avoided, and the appearance of granulation tissue and epithelium was stimulated.

Collings[10] considered that the addition of chlorophyll to an ointment of bismuth subnitrate, paraffin, and yellow petrolatum increased the rate of healing in deep burns. The addition of adrenal cortical extract to the chlorophyll and the ointment improved the results.

Boehme[4] reported experience with an ointment containing chlorophyll in the treatment of more than 50 patients with chronic ulcers of the leg which were difficult to treat. A high percentage of these ulcers healed rapidly.

The clinical experience of Bowers[6] in the treatment of a large number of patients with chlorophyll in solution and in the form of an ointment was satisfactory. He con-

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cluded that objectionable odors disappeared rapidly, that a remarkable cleanliness of the wounds was apparent, that the granulation tissue seemed to be finer in texture, firmer, and grew more rapidly, that epithelialization seemed to be stimulated, skin irritation was not seen, and adverse systemic reactions were not seen.

Langley and Morgan [15] found chlorophyll in the form of an ointment valuable in the treatment of 40 patients with dermatosis. Dramatic and complete relief from itching and burning was afforded 36 of 40 patients.

Barnes and Amoroso [3] studied the decline of the positive wound potential of minor abrasions on the fingers as an index of epithelial healing effected by various agents. Chlorophyll of the various agents used was found to exert the most marked affect on the repair of such abrasions.

Johnson [14] considered chlorophyll to offer a unique physiological approach to the topical treatment of pyoderma, burns, ulcers, and allergic sensitizations of the skin. Chlorophyll had good properties as a topical dressing since it was a biotherapeutic agent which was bland, soothing, not toxic, and stimulating to the growth of cells.

Gratifying results were achieved by Cady and Morgan [8] in the treatment of 50 patients with chronic ulcers. In the earlier cases with gross infection, penicillin was added to the ointment, but in the latter two-thirds of the series, penicillin or other antibacterial agents were not added to the ointment.

Carpenter [9] used chlorophyll in isotonic saline, chlorophyll in an ointment in a hydrophilic base, chlorophyll combined with penicillin in an ointment, and fine mesh gauze impregnated with an ointment containing chlorophyll to treat infected wounds. Remarkable healing properties were ascribed to the chlorophyll.

Lowry and Curtis [16] found that, where loss of skin in a skin graft occurred, or where the skin graft was cut too deeply, chlorophyll in an ointment could be used advantageously to promote healing. The same results were obtained in traumatic wounds of the digits in which loss of epithelium occurred.

An ointment containing chlorophyll and a solution of the substance were used by Pollock, Boshes, Finkelman, Chor, Arieff, Brown, Barber, Kostrubala, Newman, and Kesert [19] in the treatment of decubitus ulcers. Chlorophyll in these forms provided the most effective form of treatment.

Sack and Barnard [20] presented data to show that exudates from nonhealing lesions exhibited hemagglutinating properties against the red blood cells of the patient and produced inflammatory lesions when injected intradermally in the skin of the abdomen of a rabbit. When derivatives of chlorophyll were combined with the exudate from the wound, the hemagglutinating property and the inflammatory factor of the exudate were inhibited. Based on this experimental data, the concept was advanced that failure of healing of wounds often resulted from the presence of uncompensated mucoprotein of median molecular size in the exudate. These proteins agglutinated red blood cells, causing plugging of capillaries, and attacked tissue cells to cause inflammation. The beneficial effect of chlorophyll on wounds which did not heal might be attributable to the inhibition or reduction of hemagglutinating and inflammatory properties of the exudate in such wounds.

The results of the study of the healing of wounds and the deodorant effects of chlorophyll by Moss, Morrow, Long, and Ravdin [18] were interesting. They concluded that chlorophyll was not a consistent promoter of wound healing, that chlorophyll did not retard wound healing, and that chlorophyll was a consistent effective deodorant, improved the appearance of wounds, and gave them a healthy granulating appearance.

Two further factors for the successful use of chlorophyll have been delineated in the laboratory. These facets involve the reaction of fibrinogen and chlorophyll and the reaction of red blood cells and chlorophyll.

The fact that chlorophyll will inhibit the conversion of fibrinogen to fibrin by thrombin is a partial explanation of this problem.[1,17] The cause of the inhibition is not known.

The water-soluble derivatives of chlorophyll will prevent the agglutination of red blood cells by various substances of which the common factor was presumed their mucoprotein character or content.[2] The chlorophyllin inhibited the agglutination by combining with the mucoprotein or by competitively occupying the cell receptor. The evidence was in favor of the competitive phenomenon since hemagglutination could recur when the chlorophyllin was removed from the test system.

Chlorophyllin may act directly upon the red blood cells, therefore, to prevent hemagglutination. It has been stated, however, that red blood cells will not adsorb chlorophyllin from a suspension of the substance.[23] This hypothesis was examined.

A 0.0025% solution of sodium-copper chlorophyllin * in an isotonic solution of sodium chloride at a pH of 6.1 and a 0.0050% solution were made. Of these solutions 2 ml. was added to 0.2 ml. of a 4.0% suspension of washed human red blood cells in an isotonic solution of sodium chloride. Mixtures of 2.0 ml. of the solutions of sodium-copper chlorophyllin and 0.2 ml. of the isotonic solution of sodium chloride served as controls. To determine the amount of hemolysis which occurred 2 ml. of an isotonic solution of sodium chloride and 0.2 ml. of the suspension of red blood cells were used. The mixtures were incubated in a water bath at 37 C for various times up to four hours. The suspensions were shaken every 30 minutes. At the end of the period of incubation, all of the mixtures were centrifuged at 2,000 rpm for 20 minutes. The supernatant fluid was decanted into colorimeter cuvettes. With a No. 42 blue filter in place, the fluid from the suspension of red blood cells in the isotonic solution of sodium chloride was read to determine the amount of hemolysis which had occurred. This result was the correction factor and it was subtracted from the readings obtained when the fluids containing the suspension of red blood cells in the solutions of sodium-copper chlorophyllin were read. The readings of the sodium-copper chlorophyllin in the isotonic solution of sodium chloride were recorded as 100%. The difference between the readings of these suspensions and those containing the red blood cells in the solution of sodium-copper chlorophyllin was the amount of the sodium-copper chlorophyllin removed by the red blood cells. The tests were done in triplicate, and the results were averaged (Table 1). The examinations were repeated with use of Sorenson's phosphate buffer solution at a pH of 7.0 (Table 2).

* The sodium-copper chlorophyllin was supplied by the Rystan Company, Mount Vernon, N. Y.

TABLE 1.—*Amount of Sodium-Copper Chlorophyllin Removed by Washed Human Red Blood Cells in Isotonic Solution of Sodium Chloride*

Time	Amount of Sodium-Copper Chlorophyllin μg. Removed	
	0.0025% Solution	0.0050% Solution
15 min.	6.8	13.4
30 min.	8.5	15.5
45 min.	11.6	14.8
1 hr.	11.5	15.0
2 hr.	14.1	15.0
3 hr.	14.2	17.5
4 hr.	19.6	19.0

Roughly comparable amounts of sodium-copper chlorophyllin were removed from the two solutions by the red blood cells

TABLE 2.—*Amount of Sodium-Copper Chlorophyllin Removed by Washed Human Red Blood Cells in Sorenson's Phosphate Buffer Solution*

Time	Amount of Sodium-Copper Chlorophyllin μg. Removed	
	0.0025% Solution	0.0050% Solution
15 min.	6.8	13.4
30 min.	8.5	15.5
45 min.	11.6	14.8
1 hr.	11.5	15.0
2 hr.	14.1	15.0
3 hr.	14.2	17.5
4 hr.	19.6	19.0

except during the last two hours of the experiment. The reason for the increased rate of removal of the sodium-copper chlorophyllin from the solution of isotonic sodium chloride as contrasted with the Sorenson's phosphate buffer solution during this period of time is not known. The variations between the individual determinations may be due to a different number of red blood cells in each specimen since they were not counted. It is not known whether the sodium-copper chlorophyllin was present on the surface of the red blood cell or whether it entered the cell to unite with the hemoglobin or the stroma.

Summary

Sodium-copper chlorophyllin is removed from solution by washed human red blood cells. The method of the removal of the sodium-copper chlorophyllin from solution by washed human red blood cells is not known.

Surgical Service, Veterans Administration Hospital.

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Recognition and Treatment of Alterations in Ammonia Metabolism *

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As clinical and experimental knowledge of ammonia metabolism increases, the relationship between increased concentrations of ammonia in the blood and the clinical state of "hepatic coma" becomes apparent. The occurrence of significantly increased concentrations of ammonia in the blood of patients with "hepatic coma" and the clearing of the sensorium that follows a reduction of the blood ammonia concentration both indicate that ammonia intoxication is an important factor in the production of hepatic encephalopathies. Further confirmation of an etiologic role of ammonia in "hepatic coma" is to be found in the fact that this syndrome can be reproduced in both experimental animals and human subjects by increasing the blood ammonia, either by the administration of ammonium salts or by the feeding of high-protein diets or urea. In patients who have had vascular shunting procedures done for portal hypertension, or in patients in whom chronic liver disease is associated with gastrointestinal hemorrhage "hepatic coma" may also occur.

Ammonia in the blood is derived mainly from the gastrointestinal tract, where it is produced as a result of the action of intestinal bacteria on nitrogenous substrates. These substrates include dietary protein, urea, and uric acid (which are excreted in part into the gastrointestinal tract); blood that accumulates in the gastrointestinal tract may also be an important source of increased blood ammonia. Although the blood in the venous return from the colon normally contains relatively large amounts of ammonia, the liver rapidly removes it, largely by converting it to urea. Consequently there usually is little or no ammonia in the peripheral blood. Small amounts of ammonia have been reported to originate from the lungs, kidneys, and brain, but these sources are quantitatively unimportant in comparison with the ammonia derived from the gastrointestinal tract.

Because the liver has such an important role in the metabolism of ammonia, a decrease in hepatic function, or a bypass of the liver brought about by the development of portal-systemic collaterals or surgical shunting procedures may cause high concentrations of ammonia to accumulate in the peripheral blood.

The important aspects of ammonia metabolism in man are illustrated in Figures 1, 2, and 3.

The diagnosis of ammonia intoxication is dependent upon clinical signs and symptoms, electroencephalographic changes, and the determination of the concentration of ammonia in the blood and in the cerebrospinal fluid.

The results of clinical studies in 100 cases of hepatic disease associated with encephalopathy were used to construct a diagram indicating the clinical stages of encephalopathy associated with ammonia intoxication (Fig. 4).

These stages of ammonia intoxication have been classified with regard to state of

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From the Surgical Research Laboratories of the University of California School of Medicine.

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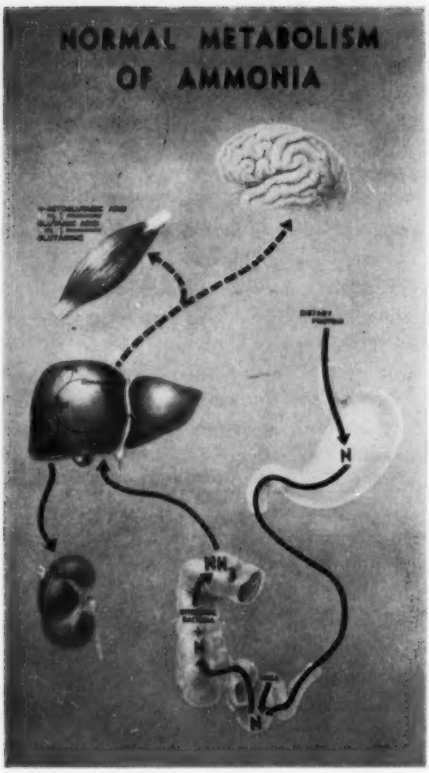


Fig. 1.—Dietary protein is the principal source of ammonia that is produced within the intestine. Urea, which is excreted in part into the gastrointestinal tract, also contributes to the production of ammonia. Both of these nitrogen-containing compounds are converted into ammonia by the numerous bacteria within the colon. The ammonia originating in the intestine is absorbed into the portal circulation, and under normal conditions is rapidly metabolized in the liver by the formation of urea, which is excreted by the kidneys. The hepatic mechanism for detoxification of ammonia is so efficient that little or no ammonia can be found in the peripheral blood of normal persons. The small amounts of ammonia that originate from the lungs, kidneys, and brain or which may escape from the liver can be metabolized in the peripheral tissues by amination reactions, as illustrated by the conversion of α-ketoglutaric acid to glutamic acid and of glutamic acid to glutamine.

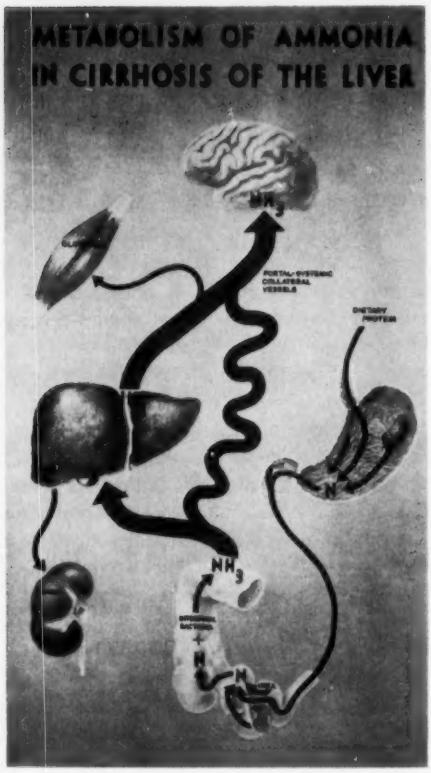


Fig. 2.—In addition to dietary protein, bleeding from esophagogastric varices, peptic ulcer, or neoplasms of the gastrointestinal tract add to the production of ammonia within the intestine and thus to the ammonia content of the portal blood. In cirrhotic patients a portal-systemic collateral circulation develops as a result of portal hypertension. Consequently, the portal blood with its high concentration of ammonia is partially diverted to the systemic circulation through these collateral vascular channels. The remainder of the portal blood enters the liver, but because of decreased hepatic function the ammonia is only partially converted to urea, so that high concentrations of ammonia remain in the hepatic venous blood. The effect of the collateral circulation accompanied by the decrease in detoxification of ammonia by the liver permits accumulation of high concentrations of ammonia in the peripheral blood. The toxic effects of ammonia can now be exerted on the central nervous system.

consciousness, motor activity, and changes in deep tendon reflexes of the patients. The onset of the delirium characteristic of the first stage may be so insidious as to escape recognition. Later these patients may become disoriented and have clinical findings ordinarily associated with alcoholic intoxication, such as slurred speech, blurred vision, and a staggering gait. Occasionally such a patient may become maniacal and irrational, with visual and auditory hallucinations. However, maniacal behavior is unusual; more often such patients are confused and gradually become drowsy. Dur-

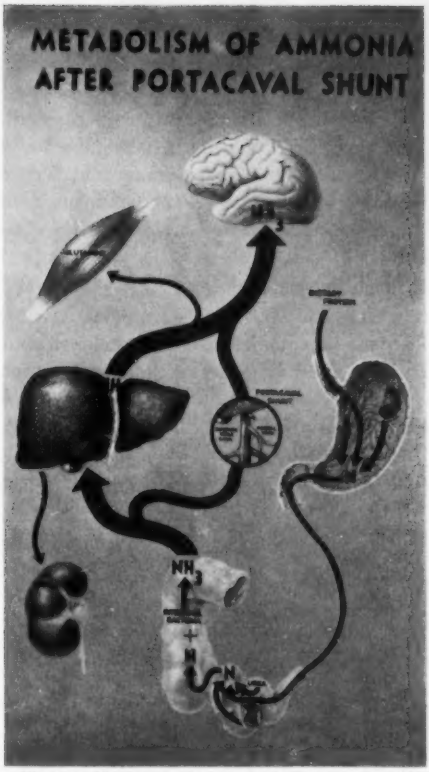


Fig. 3.—Circumstances similar to those described in patients with cirrhosis of the liver account for the increase in ammonia in the peripheral blood of cirrhotic patients in whom a portacaval shunt has been surgically produced.

ing the early stages of delirium, the patient's comprehension becomes so impaired that it is difficult for him to comply with simple requests. Response to questioning is delayed and often irrelevant. In this state the deep tendon reflexes become increasingly more active. Also a positive grasp reflex is frequently elicited. Occasionally there may be inequalities of reflex responses. (This may make it difficult to differentiate between "hepatic coma" and subdural hematoma.)

In the stage of delirium motor activity increases and is associated with marked restlessness and the development of characteristic involuntary movements. Such movements were first described by Adams and Foley, and have been designated as "liver flaps." This may be demonstrated when the patient holds his arms and hands outstretched with the fingers spread apart, at which time it appears as a series of lateral deviations of the fingers, and rapid and arrhythmic flexion-extension of the fingers at the metacarpophalangeal joints with flexion-extension at the wrists. If the patient is asked to place his hands on his head the "flap" is manifested at the elbows. This sign, while very characteristic of hepatic encephalopathy also occurs in uremia and occasionally has been reported in re-

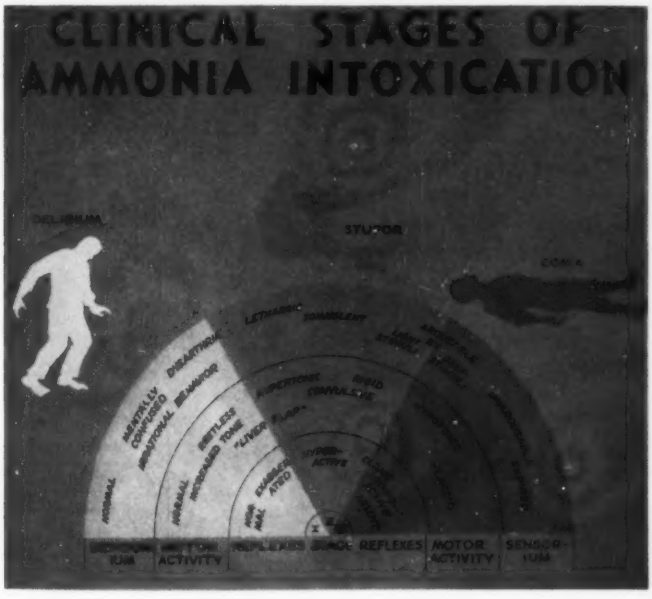


Fig. 4.—Diagrammatic representation of the three stages of encephalopathy associated with ammonia intoxication.

spiratory acidosis. The "liver flap" occurs early in the course of ammonia intoxication in patients with liver disease and can be elicited until the patient lapses into coma; however, even in a comatose patient it may be seen if his wrists are held and the movements of the hands are then observed.

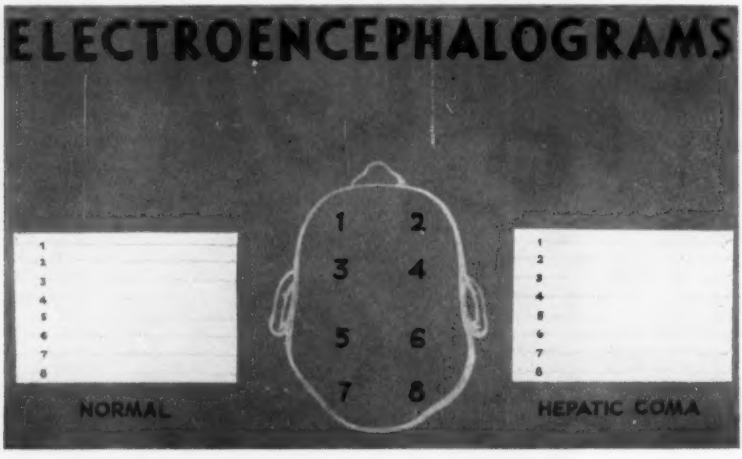
The second stage, designated as one of stupor, is characterized by progressively increasing drowsiness and lethargy. Such patients become somnolent, sleeping almost continuously but still responding to light stimuli. As the encephalopathy progresses the patient can only be aroused by stronger painful stimuli. The deep tendon reflexes become hyperactive, and in many cases ankle and knee clonus can be demonstrated. Later in this stage many of these patients develop an extensor plantar response. Then motor activity increases until they finally develop marked resistance to passive movements. Such paratonic rigidity has been observed in most of these patients during this stage. Occasionally generalized or focal convulsions occur in the late phases of the stupor.

Coma develops insidiously following stupor. Usually the onset of coma becomes apparent when the patient can no longer respond to strong painful stimuli. As coma deepens, the pupils of the eyes become dilated, respirations become stertorous and finally Cheyne-Stokes just prior to death. The hypertonic condition of the muscles is lost and they become hypotonic and finally flaccid. The reflexes also become hypoactive as coma progresses and are absent prior to death.

Electroencephalographic changes observed in patients with ammonia intoxication are not pathognomonic of this condition but may be used in conjunction with other laboratory examinations to confirm the clinical diagnosis (Fig. 5).

The concentration of ammonia in the blood may generally be correlated fairly well with the clinical progression of the encephalopathy of "hepatic coma." This is confirmed by the results of over 400 measurements of blood ammonia concentrations done in the University of California Surgical Laboratories on the peripheral venous blood of patients with "hepatic coma." A similar conclusion was reached by Phear et al., who reported a more than 90% correlation between the blood ammonia concentrations and the neurological status of the patients in a series of 366 measurements of concentrations of blood ammonia.

Fig. 5.—An illustration of the electroencephalographic pattern obtained with the eight parasagittal leads comparing a normal subject and a patient in "hepatic coma." The alterations in the electroencephalographic pattern of this patient in "hepatic coma" show paroxysms of random high voltage asynchronous slow wave activity on a background of normal activity.



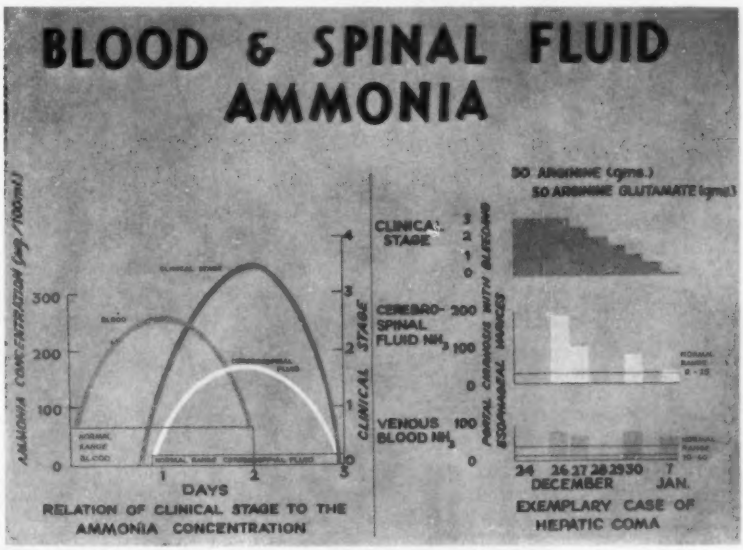
The concentration of ammonia in the peripheral blood has in the past usually been determined by the microdiffusion technique of Conway; more recently the analytical method of Seligson has been used. Determination of ammonia concentrations can be done in about 30 minutes by any qualified laboratory technician, and the equipment that is necessary to make these determinations is relatively simple and inexpensive.

In approximately 10% of cases the concentration of ammonia in the venous blood did not correlate well with the clinical findings in patients with hepatic encephalopathy due to ammonia intoxication. This lack of correlation between the blood ammonia concentrations and the severity of symptoms is the basis for conflicting opinions on the etiologic significance of increased blood ammonia concentrations in "hepatic coma." Recent work in this laboratory has shown that there is a closer correlation between the clinical stages of hepatic encephalopathy and concentrations of ammonia in the cerebrospinal fluid than with blood ammonia concentrations. It is possible that the cerebrospinal fluid concentrations of ammonia reflect more closely the cerebral tissue concentration of ammonia (Fig. 6).

Measurement of the concentration of spinal fluid ammonia may therefore be used as additional laboratory confirmation of ammonia intoxication when the blood ammonia concentration does not correlate with clinical status of the patient. The technique for measurement of spinal fluid ammonia is the same as that used to determine blood ammonia concentrations.

Treatment of ammonia intoxication is directed toward reducing the amount of ammonia entering the portal circulation and lowering the levels of ammonia in the systemic blood. The production of ammonia in the gastrointestinal tract of patients with severe liver disease can be controlled by (1) limitation of the intake of protein, (2) control of gastrointestinal bleeding, (3) prompt removal by catharsis or lavage of

Fig. 6.—Graph showing (1) the relationship between peripheral venous blood and cerebrospinal fluid ammonia concentrations and the clinical stage of hepatic encephalopathy, and (2) an exemplary case to illustrate the comparison of the blood and cerebrospinal fluid ammonia concentrations in a patient with "hepatic coma" and ammonia intoxication caused by bleeding esophageal varices associated with Laennec's cirrhosis. In this patient it appears that the clinical stage of "hepatic coma" correlated more closely with the concentration of ammonia in the cerebrospinal fluid than with that in the peripheral venous blood.



blood which may have accumulated from hemorrhage, and (4) oral administration of antibiotics to diminish the numbers and activities of the intestinal bacteria which produce ammonia from nitrogenous substrates. Furthermore, the administration of ammonium salts or of resins containing ammonium or of acetazolamide (Diamox) or chlorothiazide (Diuril) must also be avoided in these patients.

In order to decrease the amount of nitrogenous substrates in the gastrointestinal tract, complete removal of protein from the diet is essential during the acute phase of ammonia intoxication. After the acute phase, dietary protein may be increased gradually, using as a criterion of tolerance the effect of the additional protein on the blood ammonia. In cases of chronic ammonia intoxication secondary to surgically constructed vascular shunts, or large portal-systemic collateral shunts in association with long-standing cirrhosis, it may be necessary to maintain a decreased protein intake permanently to avoid recurrence of symptoms. In such cases the dietary protein intake need not exceed 0.5 gm. per kilogram body weight. A positive nitrogen balance may be maintained at this reduced level of dietary protein if all of it is of nutritionally excellent quality.

When gastrointestinal hemorrhage is the cause of ammonia intoxication the source of bleeding must be sought and controlled. This may be difficult because even though the diagnosis of severe liver disease has been established, the exact source of the bleeding may not be known. In addition to the history and physical examination, an emergency gastrointestinal study by x-ray or an esophagoscopy (if these procedures are possible) may be needed to establish

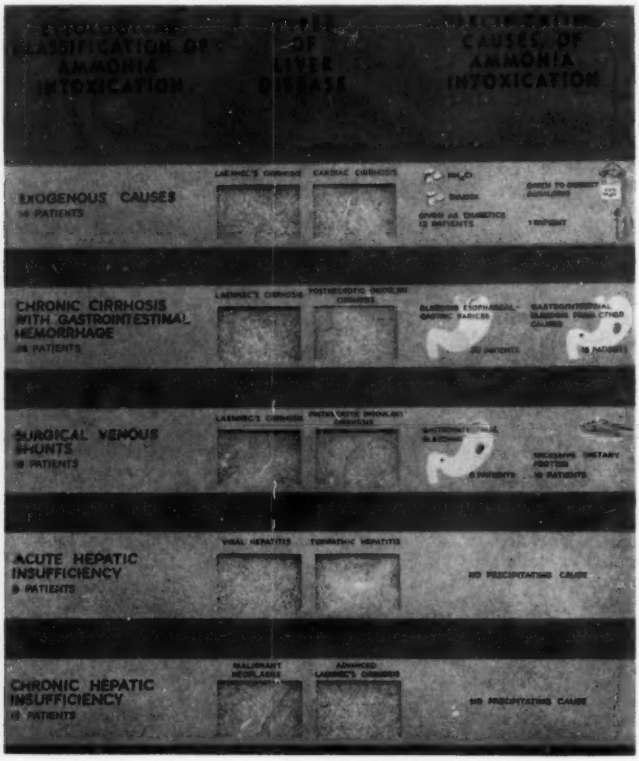
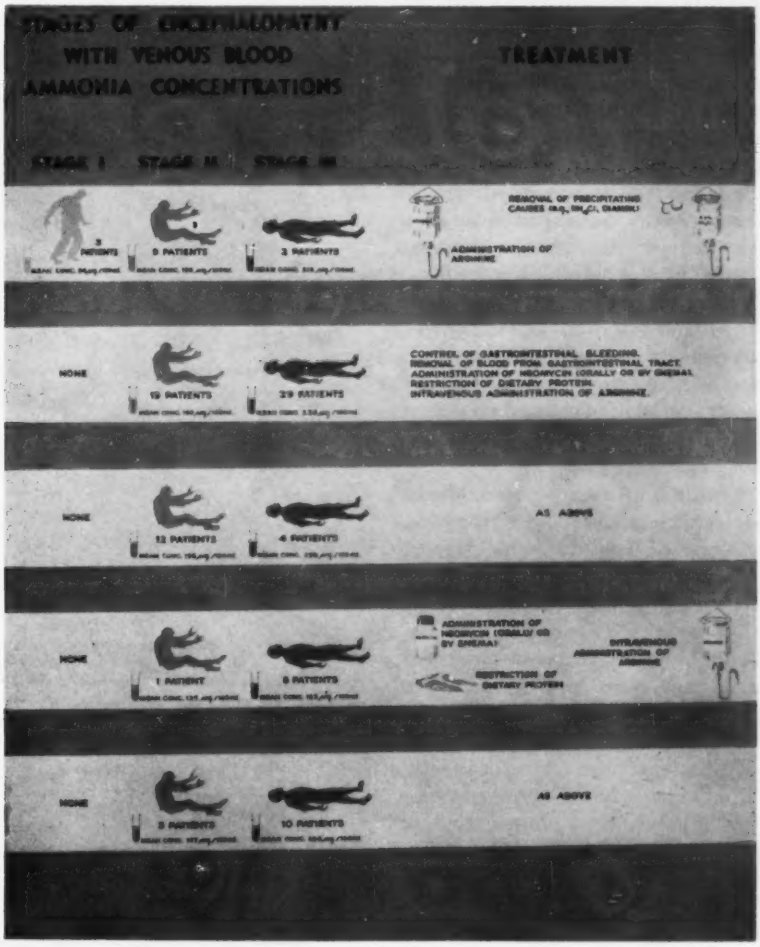


Fig. 7.—Illustration of the causes of ammonia intoxication in a series of 100 patients with various types of liver disease.

the diagnosis. When a diagnosis of bleeding esophageal varices is made or strongly suspected, treatment with the Sengstaken esophageal compression balloon should be attempted. Surgical control of bleeding esophageal varices may have to be done as an emergency procedure if the bleeding has not been controlled by esophageal tamponade. Other causes of gastrointestinal hemorrhage, such as peptic ulceration, hemorrhoids, neoplastic disease, and blood dyscrasias, should be treated with appropriate methods if continued bleeding which cannot be controlled by conservative measures occurs. Regardless of the cause of bleeding, the blood accumulated within the gastrointestinal tract must be removed as soon as possible. For this purpose, gastric lavage and enemas are effective. During the acute phase of ammonia intoxication, the removal of blood from the gastrointestinal tract can also be expedited by the use of a mild cathartic such as 30 cc. of milk of magnesia four times daily administered by indwelling nasogastric tube.

Fig. 8.—Illustration of the stages of encephalopathy and venous blood ammonia concentration in five etiologic classifications of ammonia intoxication. The treatment of each is shown.



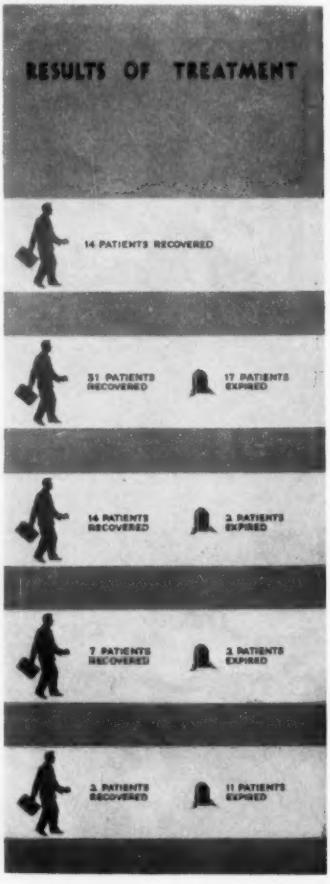
The oral administration of antibiotics to reduce the intestinal flora is as important as the other measures used for control of ammonia production within the gastrointestinal tract. Neomycin appears to be the most effective antibiotic for this purpose. It should be given orally or by nasogastric tube in doses of 1 to 1.5 gm. every six hours. The clinical and biochemical response of the patient will determine the duration of neomycin therapy. This period is usually between four and seven days. Examination of the patient's urinary sediment should be done daily to detect promptly the occurrence of manifestations of nephrotoxicity. In some cases enemas of a 1% solution of neomycin may be an effective method for rapid intestinal sterilization.

Although the control of the production of ammonia in the gastrointestinal tract is effective for the treatment of ammonia intoxication, a rapid lowering of the blood ammonia is essential to prevent irreversible brain damage when the patient is in stupor or coma. Methods to lower the blood ammonia have usually involved attempts to enhance the reactions by which ammonia is metabolized and removed from the body. The rationale for therapy of ammonia intoxication with glutamic acid proposed by McDermott and Walshe is based on removal of ammonia by amidation of glutamic acid to form glutamine.

The formation of urea is, quantitatively, the most important method by which ammonia is removed from the body. Although this reaction occurs only in the liver, investigation has shown that experimental removal of 80% to 90% of the liver does not significantly alter urea production. Similar findings were reported in experiments in which livers removed from dogs were perfused with a toxic agent such as CCl_4. The extreme degree to which hepatic function must be reduced before urea production is affected was confirmed clinically by the ability of arginine to lower blood ammonia significantly and to raise the blood urea in patients with what has been described as "massive hepatic necrosis."

In the Experimental Surgery Laboratories of the University of California it has been demonstrated that intravenously administered arginine significantly lowers high levels of ammonia in the blood, both experimentally and clinically. Comparative studies of the effectiveness of arginine and of glutamic acid in the treatment of experimentally induced ammonia intoxication confirmed the superiority of arginine in lowering high blood ammonia levels rapidly and effectively. The decrease in the level of ammonia in the blood following the administration of arginine was always accompanied by a significant rise in the blood urea

Fig. 9.—Diagram showing the results of treatment for each of the five classifications of ammonia intoxication illustrated in Figure 8.



nitrogen, suggesting that arginine exerts an effect on the blood ammonia because of its role as a precursor of ornithine in the Krebs-Henseleit cycle in the liver.

Arginine was administered intravenously to patients with ammonia intoxication as arginine hydrochloride or arginine glutamate.† Each dose consisted of 500 cc. of a 5*7*% solution of arginine in 10% dextrose administered over a two-hour period. At least 8 to 12 hours was allowed to elapse before the second dose was given, because it was found that serum arginine levels remained high for 8 to 12 hours after administration of 25 gm. of the amino acid. No toxic effects have been observed after more than 200 intravenous infusions of arginine in a series of 90 patients.

The basic etiological factors and precipitating causes of ammonia intoxication as well as the stages of encephalopathy of 100 patients with ammonia intoxication are described in the next three panels; the treatment and the results are also shown in Figures 7, 8, and 9.

University of California School of Medicine (*22*).

†Obtained from Abbott Laboratories, Cutter Laboratories, and Merck Sharp & Dohme.

Method for Removal or Debridement of Burn Wound Eschar

WILLIAM SCHUMER, M.D., Chicago

One of the most difficult problems in the care of the burn wound begins with the first change in dressing. At this time, the surgeon is faced with the problem of deciding the method for debridement of the burn wound. This eschar is composed of necrotic skin destroyed by the burn, coagulated protein from the exudated plasma, and bacterial exudates which have begun developing. Normally the eschar loosens about the second or third week, and underneath the eschar the granulation base appears. However, the sooner this granulation base develops, the earlier a graft can be applied.

The surgeon has three alternatives in the debridement of the eschar. He may wait until normal separation of the eschar occurs, application of dry dressings, or he may decide on surgical (mechanical) debridement. The third method is applying wet saline soaks. The disadvantages to the first dry-dressing method is the length of time necessary for separation of the eschar. The extended length of time is detrimental to the optimum grafting time. Surgical excision of the eschar may result in hemorrhage and marked loss of blood volume and this may be decisive, especially in extensive burns. One also fears the necessity of anesthesia during the surgical debridement. Consequently, the wet-soak technique is probably the best of the three methods. However, wet saline should be applied every four hours, and this method is time-consuming and requires a great deal of nursing care.

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There is still another method which was introduced in 1860 by Van Hebra. This is the hydrotherapeutic technique of removing the burn wound eschar. At Mount Sinai Hospital the method has been implemented by use of the Hubbard whirlpool tank. Usually, the first dressing is changed after the fifth day, when the compression pads are removed, if there is no adherence to the eschar. The inner petrolatum dressings and adherent compression pads are allowed to remain on the patient. The patient is then immersed in the water of the Hubbard tank. The water may be mixed with hexachlorophene soap. The dressings are gently removed or allowed to soak off. The patient remains in the water for 20 to 25 minutes. During this time the whirlpool action of the air jets of the Hubbard tank is utilized. The patient is then redressed with sterile petrolatum gauze and compression pads. This process is repeated every day or every second day, until the granulation base necessary for grafting is developed. This usually takes 7 to 10 days after the burn day, depending on the extent of the burn.

This technique has certain advantages over the three generally accepted methods described above. For one thing, the eschar debrides much more quickly, as much as 7 to 10 days faster, as exemplified by the case described below. This technique of debridement is extremely gentle, and we have never seen any hemorrhage develop during these tank immersions. The use of the air jet, which causes strong eddies in the water, gives us the advantage of mechanical debridement. The debridement is certainly more comfortable for adults, and actually fun for the children. The general

purpose of the Hubbard tank, to aid in the motion of joints, is another advantage in preventing contractures. The only disadvantage one considers when studying the above method is the fact that one is placing a sterile wound in water that is not sterile, even with the hexachlorophene soap. The only answer to the above is the experience with this method. Bacterial exudates have ceased to be the problem they previously were, and the granulation areas are healthy as evidenced by the per cent "take" we have with this method. Apparently, the constant cleansing with the water and mechanical debridement via the air jet, does not encourage any further infection. This has already been proved by the culture method on the granulation tissue and taking the pH of the granulation. An example of the clinical application of this method occurred in the following case:

A 6-year-old boy incurred a second- and third-degree burn of the lower one-third of his abdomen, anterior and posterior, and his lower extremities, anterior and posterior. The burn wounds were cleansed, and a compression bandage was applied. General fluid therapy was adequate, and the patient did well until the fifth postburn day, when the bandages became extremely odoriferous. He was taken to the Hubbard tank, and the outer shell dressings were removed. He was then immersed in the water and after gentle removal of the petrolatum dressings, it was found that he had a greenish exudate over most of the wound, which culture revealed to be Staphylococcus aureus and Pseudomonas aeruginosa. After four days of 20-minute hydrotherapeutic immersions and redressings, the exudate had completely disappeared and the eschar had also been debrided. On the ninth postburn day, the granulation base over the abdomen, inguinal area, and thighs was adequate for grafting, in spite of previous infection. The graft was applied on the 10th postburn day, and the take was adequate (85%).

Because of the lack of donor skin and inability to get permission for homograft, the legs were not covered. However, the granulation areas were kept adequate with the continued use of the small whirlpool tank, the legs being carefully immersed in order not to moisten the graft bandage. The patient was again ready to be grafted in 7 to 10 days.

The above example is not unusual. We have treated 35 burn wounds with the same technique described, and all the results have been excellent as regards the time required for the debridement of the eschar and the feasibility of the method.

Summary and Conclusion

Our experience with a technique for the debridement of the burn wound eschar by use of hydrotherapeutic methods has been described, and we encourage its adoption.

My grateful acknowledgement to Dr. G. Davidson and the Department of Physical Medicine for their aid in preparing the material for this manuscript.

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Surgical Wound Infection in a Thoracic Disease Hospital

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In recent years much has been written regarding the occurrence of staphylococcal infections in various institutions. Whether this is due to increased awareness or to an actual increase is difficult to estimate. Whatever the incidence, it cannot be denied that epidemics of infection have occurred in a number of hospitals; and it is the purpose of this communication to report such an epidemic together with the corrective measures and bacteriological data.

Ray Brook State Tuberculosis Hospital is situated in a relatively isolated part of the Adirondack Mountains. It accommodates an approximate census of 300 patients, who are drawn principally from the northern counties of New York State and New York City. Surgery is principally thoracic for pulmonary tuberculosis, pulmonary resection being the most commonly performed procedure. Other surgery, including abdominal and orthopedic, is performed when necessary, but such procedures are relatively few. With few exceptions the surgery is performed by the same two surgeons who are regular staff members. Other operating room personnel are regular employees, with the exception of two anesthetists who also serve the surrounding communities. Because of its isolation and unchanging surgical personnel, this hospital proved an ideal location in which to study the epidemiology and control of surgical wound infections.

In spite of almost routine postoperative administration of aqueous penicillin and occasionally other antibiotics such as tetracycline, erythromycin, chloramphenicol or streptomycin, in the year 1956, 10% (13) of 132 clean major surgical wounds became infected, an incidence which greatly exceeds that which is generally accepted. This occurred in spite of sporadic attempts to improve results. In January and February, 1957, of 13 clean major surgical wounds 4 became infected. Although these infections involved only the superficial tissues in all but one instance, this alarming increase called for a drastic revision of procedure incorporating as many features as possible which had been reported by others to be beneficial.

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Changes in Procedure

Coincident with other changes the installation of an air conditioner in the operating room suite was completed in February, 1957. This supplied fresh filtered air from the outside at the rate of approximately one change every three and one-half minutes at a slightly positive pressure.

In spite of the fact that routine culturing of sterilized material had failed to reveal evidence of bacterial contamination, techniques of sterilization were reviewed and revised. Whenever possible steam sterilization was prescribed. Great care was exercised to insure contact of steam with all surfaces of material to be sterilized. Chemical sterilization was reduced to a minimum. Boiling was eliminated except for the sterilization of polyethylene beads used for plombage thoracoplasty, since their melting point was too low to permit autoclaving.

The number of visitors in the operating room was reduced as much as possible.

Those who entered were required to change into operating-room clothing. Woolen blankets and clothing were excluded since they are difficult to sterilize. Freshly laundered cottons were substituted as they had been shown to be relatively free from bacterial contamination.[1] Drapes were handled carefully to reduce the formation of air currents. Personnel with severe colds or skin infections were relieved from duty. Talking in the operating room was reduced to a minimum. The thickness of gauze masks was doubled and occasionally tripled. The masks were changed every hour and a half. The patient's nose and mouth were carefully covered until endotracheal tube or anesthesia mask could be substituted. These precautions were carefully observed between surgical cases. Moreover, between operations and when the operating room was not in use it was closed to all but necessary traffic. If for some reason it became necessary for someone to enter the operating room in street clothing or without masks, the room was not used for surgery for 24 hours subsequently.

Large "splash" basins for washing the hands were considered dust catchers and replaced by a single wide-mouth pitcher which could be covered. No suction equipment was permitted which was not connected to pumps outside the operating room. Surgical hand scrubbing was prolonged to 10 minutes with hexachlorophene (pHisoHex) for all operations. Evidence that rubber gloves had been punctured was carefully watched for by the scrub nurse, and when this occurred gloves were immediately changed.

The only major change in surgical technique was the substitution of a continuous absorbable subcuticular suture for interrupted through-and-through skin silks, which were found often to interfere with local circulation, thereby predisposing to infection.

The results of these changes became apparent almost immediately. Since their adoption there has been only one wound infection in over 150 clean major surgical operations. Moreover, since that wound infection occurred after an appendectomy and

TABLE 1.—*Clean Surgical Wound Infections*

Date of Operation	Type of Operation	Organism Recovered	Sensitivity *							Postoperative Antibiotics
			P	C	T	A	E	S	SS	
1/20/1956	Pulmonary resection	S. albus				R		R	R	Penicillin (1,000,000 u q 4h)
2/17/1956	Pulmonary resection	S. albus	R							Penicillin (1,000,000 u q 6h)
3/12/1956	Pulmonary resection	S. albus								Penicillin (1,000,000 u q 4h)
4/11/1956	Pulmonary resection	S. aureus								Penicillin (500,000 u q 6h)
4/18/1956	Plombage thoracoplasty	S. albus						R	R	Penicillin (500,000 u q 6h)
5/16/1956	Plombage thoracoplasty	P. pyocyanea							R	Penicillin (1,000,000 u q 4h)
5/21/1956	Pulmonary resection	S. albus	X	X	X	X	X	X	X	Penicillin (1,000,000 u q 4h)
6/ 4/1956	Pulmonary resection	Staphylococcus							R	Penicillin (500,000 u q 6h)
7/26/1956	Cholecystectomy, common duct exploration, appendectomy	S. faecalis	R	R	R	R	R	R	R	Penicillin (500,000 u q 6h)
		Unidentified Gram-negative bacillus	R	R			R	R		
9/18/1956	Plombage thoracoplasty	B. proteus					R		R	Penicillin (1,000,000 u q 4h)
9/26/1956	Pulmonary resection	S. aureus								Penicillin (1,000,000 u q 4h)
10/ 8/1956	Pulmonary resection	S. albus							R	Penicillin (1,000,000 u q 6h)
10/12/1956	Pulmonary resection	S. albus								Penicillin (500,000 u q 6h)
1/18/1957	Pulmonary resection	S. albus			R					Penicillin (1,000,000 u q 6h)
1/21/1957	Pulmonary resection	S. albus			R					Penicillin (1,000,000 u q 4h)
1/23/1957	Pulmonary resection	S. albus			R					Penicillin (500,000 u q 6h)
2/ 6/1957	Pulmonary resection	S. albus						R	R	None
10/16/1957	Appendectomy	Unidentified Gram-negative bacillus	R						R	None

* R indicates resistant; X, no determination made; blank spaces indicate organisms to be sensitive to the drug indicated at the top of the column; P, penicillin; C, chloromycetin (chloramphenicol); T, terramycin (oxytetracycline); A, aureomycin (chlortetracycline) E, erythromycin; S, streptomycin; SS, triple sulfa. (trisulfapyrimidines).

was due to an unidentified Gram-negative bacillus, it may be assumed that the source was the patient's bowel.

Possible Sources of Wound Infections

Table 1 summarizes pertinent data regarding wound infections which occurred between Jan. 1, 1956, and Nov. 1, 1958. Cultures and drug sensitivity tests were performed by the disk method, using Desi Disks * on blood-agar Petri dishes which are incubated for 24 hours at 37 C. Most of the infections were due to Staphylococcus albus (Micrococcus pyogenes var. albus) in contrast to the high incidence of Staphylococcus aureus (M. aureus) reported by others. This is what might have been expected if the source of infection was the upper respiratory tract, since repeated nose and throat cultures of operating room personnel yielded S. albus in all instances but S. aureus much less frequently. That the respiratory tract was not the only possible source of infection is indicated by the fact that the three wound infections which occurred in January, 1957, were due to S. albus, which demonstrated the same drug sensitivity pattern as the same type of organism recovered from a chronic innocent-appearing lesion on the skin of a staff member working in the operating room suite. It is interesting that this individual was not a member of the operating team. The infections which occurred in the plombage thoracoplasties may have resulted from incomplete sterilization of polyethylene beads which had been boiled. It is not surprising that wound infections in the abdominal operations were due to Streptococcus faecalis and Gram-negative bacilli, indicating the probably source to be the gastrointestinal tract.

It is interesting that with only four exceptions the patients listed in Table 1 received postoperative prophylactic penicillin to which the infecting organisms were sensitive. Since aqueous penicillin was administered parenterally, there is every reason to believe that tissue antibiotic levels were relatively high. It would appear, therefore, that, although salutary, antibiotics cannot guarantee freedom from infection.

Concomitant with revision of operating room routines, the bacteriological studies to be described were initiated to further investigate possible sources of wound infection.

Bacteriological Data

Nutrient blood agar plates were exposed near the field of operation during the course of 122 procedures. These were incubated at 37 C for 24 hours, after which the number of colonies was counted and the organisms identified. The number of colonies was divided by the time of exposure to obtain the colony count per hour. With few exceptions, when Bacillus subtilis, S. aureus, and diphtheroids were found, the organism recovered was S. albus. Since B. subtilis was not recovered from the respiratory tract of operating-room personnel or patients [2] and since that organism is commonly found in the soil, it might be assumed that the organism was carried into the operating room on the shoes. Diphtheroids probably originated from the upper respiratory tract where they most frequently occur. The sources of the Staphylococcus required further investigation.

Table 2 indicates the monthly bacterial counts determined by the method described in the preceding paragraph. Generally, air pollution was higher in winter than in summer, which Hart [1] attributed to the higher

TABLE 2.—*Bacteriology of Operating-Room Air by Month*

Month	Colony Count per Hour	Month	Colony Count per Hour
April, 1957	10	Jan., 1958	19
May, 1957	7	Feb., 1958	11
June, 1957	9	March, 1958	11
July, 1957	12	April, 1958	13
Sept., 1957	7	May, 1958	11
Oct., 1957	15	Aug., 1958	10
Nov., 1957	14	Sept., 1958	10
Dec., 1957	17		

* Manufactured by the National Bio-Test, Inc.

incidence of upper respiratory infections during winter.

The average colony count per hour in the operating room was 13 for 33 operations when face masks were changed every one and one-half hours, and the same for 72 operations when masks were not changed. When standard-thickness gauze masks were worn the average hourly colony count was 10 for 19 operations. When double or triple gauze masks were worn the average hourly count was 12 for 85 operations. Metal masks were constructed and connected to wall suction with tubing to carry off expired air. Because they were uncomfortable, the latter could be tested on only one occasion, when the colony count per hour was 11. It is difficult to explain these results except by the hypothesis that air escaping between the mask and face was a greater contributor to air pollution than that which traversed the masks. If this be so, one might justifiably question the value of tests based upon the results of holding Petri dishes in front of the worn mask.

The average hourly colony count in the operating room was 13 for 16 operations when one to three visitors were present in addition to the usual personnel. The average hourly colony count was 12 for 105 operations performed without visitors. This does not necessarily indicate that the number of persons in the operating room is unimportant. It probably does indicate that if visitors are carefully dressed and instructed in proper behavior as many as two or three do not create a measurable increase in air contamination.

Though every effort was made to reduce talking in the operating room to a minimum, the actual amount of talking which did occur varied to some extent. A rough estimate of the amount was recorded after 111 operations, as 1+ to 4+. During 58 operations when talking was considered 2+ or less the average hourly colony count was 12; during 53 procedures when talking was considered more than 2+ the average hourly colony count was 13. This slight difference certainly does not mean that unlimited talking may be permitted with impunity. It merely seems to indicate that if an effort is made to control talking it is possible to avoid a serious increase in the extent of air pollution.

Petri dishes exposed on various occasions for a total of 89 hours in the unoccupied operating room yielded only eight colonied of S. albus and B. subtilis. In 45 operations lasting over three hours the average hourly colony count by the same method was 11. In 77 operations lasting under three hours the average hourly colony count was 13. Hourly colony counts obtained during several short operations were within the same range as those for longer procedures, indicating that a plateau is reached within the first hour of occupancy. Since Petri dishes exposed in an unoccupied operating room after previous occupancy yielded few organisms, it also appears likely that air pollution rapidly subsides in a properly air-conditioned room. Blood-agar plates were also exposed in the unoccupied operating room while a current of air from an electric fan was directed upon the floor, which on several occasions had not been mopped after previous surgery. The yield during a total plate exposure time of approximately 29 hours was 12 colonies of S. albus and B. subtilis. It does not appear, therefore, that the floor was a major source of air contamination.

A number of white cotton coats which had been worn on the wards and operating room clothing which had been used recently were hung upon a clothes tree in the unoccupied operating room and a stream of air from an electric fan was directed through them. Agar plates, exposed for eight hours under these conditions, yielded nine colonies of S. albus and B. subtilis. This evidence does not indicate that cotton clothing plays a dominant role in the production of air pollution.

Although the above data strongly suggest that air pollution is derived to a great extent from the respiratory tract of the operating room occupants, there remain two other obvious possible sources of contamination,

the patient's skin and the surgeon's hands. The patient's skin near the operative incision was cultured before and after surgery on five occasions by wiping with a moist sterile pledget which was then incubated in nutrient broth for 24 hours at 37 C. The patient's skin was routinely cleansed with hexachlorophene followed by ether, iodine tincture, and alcohol 70%. No organisms were recovered on five occasions prior to surgery or on nine occasions following surgery, even though two operations lasted over six hours. The hands of the operating team were cultured in a similar manner immediately after scrubbing with hexachlorophene for 10 minutes and at the completion of surgery. S. albus was recovered in 12 of 25 cultures obtained prior to surgery, and 17 of 29 cultures obtained after surgery. The incidence of positive cultures obtained after a scrubbing for a second operation was 8 out of a total of 10. These results tend to shake one's confidence in the efficacy of hand scrubbing.

Comment

The results of these studies agree to a remarkable extent with those reported by Hart.[1] Consideration of the data presented would lead one to the conclusion that a major source of wound infection is the operating-room air, which derives its bacteria from the upper respiratory tract of the occupants. Another potent source of infection is the hands of the operating team. Clothing, provided it is freshly laundered cotton, the patient's skin, and the floor do not seem to be important sources. The patient's bronchus at operation rarely contains organisms.[2] It appears that, provided the operating room is properly air-conditioned, a limited number of visitors may be permitted and a small amount of talking may be indulged in without measurably increasing the risk of wound infection.

Air pollution in a properly air-conditioned room seems to reach a maximum level within the first hour of occupancy, and to decrease as rapidly when the room is unoccupied. Although strict application of modern techniques tends to reduce the incidence of wound infection, it does not prevent air pollution. The latter can possibly be reduced further by the adoption of a specially designed transparent plastic headgear similar to a diving helmet, with an inlet valve and an exhaust connected to wall suction. Certainly, there is much need for improvement if we are to attain the ideal of asepsis.

Contrary to the experience of many others, our wound infections were due to S. albus, and these organisms were sensitive to penicillin in almost every instance. The fact that infections occurred in spite of the postoperative prophylactic administration of large doses of penicillin supports the opinion that antibiotics are not a substitute for good operating-room technique. Although penicillin has been used prophylactically after almost every major thoracic operation performed in this hospital for several years, the incidence of penicillin-resistant organisms recovered from infected wounds has been low. It appears to us that possibly the role of prophylactic use of antibiotics as a cause of increased occurrence of antibiotic-resistant organisms may have been overemphasized. On the other hand, a possibly more important source of organisms resistant to antibiotics may be the upper respiratory tract of hospital workers who indiscriminately use antibiotics for minor upper respiratory infections.

Finally, since the epidemic of surgical wound infections in February, 1957, forced us to seek an immediate solution to the problem, it was not possible to evaluate each change in procedure separately. It is difficult, therefore, to determine which of the changes accounted for the great diminution in the incidence of wound infection. Possibly the greatest factor may have been the increased awareness of the possibilities of bacterial contamination and the strict appli-

cation of known techniques which was thus elicited.

Summary

An epidemic of staphylococcal infection in clean surgical wounds is reviewed.

Organisms were most frequently Staphylococcus albus which were penicillin-sensitive.

The commonest sources of surgical wound infection are thought to be the skin and upper respiratory tract of the operating-room personnel.

By revision of operating-room procedure the incidence of surgical wound infection has been almost eliminated.

Ray Brook State Tuberculosis Hospital.

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Brain Abscess and Osteomyelitis Following Skull Traction

A Report of Three Cases

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Skeletal traction, obtained by attaching metal tongs to the skull, has been used in the management of fracture-dislocations of the cervical spine since 1933.[1] This method of treatment has proved to be useful in reducing the dislocation as well as maintaining proper alignment of the spine during healing. The occurrence of infection due to the tongs does not appear to be a serious problem even though the traction device usually remains in the skull over a long period. Only one case could be found in a review of the literature. This was an instance of osteomyelitis of the skull which occurred in a patient who was being treated with skull traction for osteomyelitis of the cervical spine.[2] Our own experience indicates that the incidence of septic complications is probably greater than the literature shows. During the period from January to November, 1958, we had occasion to treat three patients with severe infections of the skull or brain following the use of skull tongs. These cases are reported to call attention to the possibility of septic complications in patients in whom skull traction is being maintained. This report is not intended to detract from the established value of skull traction in the treatment of patients with injuries of the cervical spine.

Report of Cases

CASE 1.—A 38-year-old man was in an automobile accident and received a fracture-dislocation of the sixth cervical vertebra; compound fractures of the phalanges of the right hand, and a head injury. He regained consciousness shortly after admission to another hospital. Crutchfield tongs were attached to the skull and 18 lb. of traction added to reduce the dislocation. He remained in continuous traction for the following two weeks, at which time the tongs were removed. All the details of his hospitalization are not known. He developed a septicemia with fever and delirium, and a hemolytic Staphylococcus aureus was isolated from the blood. He was treated with penicillin, oxytetracycline, chloroamphenicol, streptomycin, erythromycin, and oleandomycin. He continued to have fever, and 51 days after injury he was transferred to our care.

Examination: The blood pressure was 120/76, respiratory rate 22, pulse rate 108, and temperature 100.8 F. The patient appeared chronically ill. There were two scalp wounds which corresponded to the site of insertion of the tong points. These wounds were open and filled with granulation tissue. There was a cellulitis of the surrounding scalp, and pus

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Fig. 1.—Lateral roentgenogram of the skull showing areas of osteomyelitis around sites of insertion of tongs in the parietal region. The irregular radiolucent areas in the posterior portion of the frontal bone are also due to osteomyelitis. The curved line seen across the frontal region is an artefact.

could be expressed from each wound. Movements of the neck were limited and painful. The neurologic examination was unremarkable.

The values for the hemoglobin and hematocrit were 12.2 gm. and 36.5%. The white blood count was 17,950 per cubic millimeter, with a differential of 86% polymorphonuclear leukocytes, 8% lymphocytes, and 6% monocytes. Hemolytic S. aureus was cultured from the scalp wounds. This organism was sensitive to ristocetin, oleandomycin (Matromycin), and novobiocin. Roentgenograms of the skull showed an irregular radiolucent area in each parietal bone which represented the site of insertion of the points of the tongs (Fig. 1). In addition, the left frontal, temporal, and parietal bones contained numerous irregular radiolucent areas. Roentgenograms of the cervical spine showed good alignment of the vertebrae and an old compression fracture of the body of C6.

He had intermittent fever as high as 102.2 F during the first 14 days of hospitalization. During this time, he received ristocetin, novobiocin, and penicillin. A total of six cultures showed no growth. The patient was seen in consultation by the neurosurgical service, and a craniectomy was advised. Immediately prior to the operation, a lumbar puncture was performed. The pressure was 300 mm. H_2O; the fluid was sterile, and the cellular pattern was normal.

A bilateral parietal craniectomy was carried out 14 days after admission. The involved bone at the site of insertion of the tongs was removed, leaving a circular bony defect about 4 cm. in diameter on each side. From the extradural space on the left 10 cc. of thick odorless pus was evacuated. The dura mater was intact.

The patient was worse after surgery. He became lethargic and his fever spiked up to 105 degrees F. A second lumbar puncture was done 48 hours after operation. The spinal fluid contained 8,000 white blood cells per cubic millimeter, the majority of which were polymorphonuclear leukocytes. Pseudomonas aeruginosa was cultured from the fluid. He was started on chloroamphenicol in addition to the other antibiotics.

His condition deteriorated without the development of focal neurologic signs. Five days after the first operation, a second craniectomy was performed on the left side, and more involved bone was removed. A total of five small extradural abscesses were evacuated. During the operation, the blood pressure fell to 60/40 mm. Hg., and despite blood transfusion and intravenous hydrocortisone, he failed to respond and died six hours later. The significant autopsy findings were as follows:

1. An extensive early ischemic necrosis of the left cerebral hemisphere in the distribution of the middle cerebral artery

2. Approximately 200 cc. of clotted blood in the extradural space on the left side

3. A 2 cm. abscess in the lower lobe of the left lung

4. No evidence of subdural or intracerebral infection

Case 2.—A 38-year-old man received a fracture-dislocation of the fifth cervical vertebra in an automobile accident. He was hospitalized elsewhere, and Crutchfield tongs were attached to the skull. The exact details of his hospital course are unknown. He stated that he was able to move all extremities at the time of admission to the hospital. Continuous skeletal traction was maintained for one month, at which time the tongs were removed. He was discharged shortly thereafter.

He was admitted to our care two months later with a four-day history of anorexia, headache, fever, stiffness of the neck, and weakness of the right extremities.

A review of the past history revealed that the patient had experienced numerous episodes of earache associated with a discharge from the left ear for 16 years. A radical mastoidectomy was performed on the left side six years after the onset of symptoms but without relief. He had noted a slight discharge from his left ear, which was not associated with pain, for two weeks before admission to our hospital.

Examination: The blood pressure was 120/75, respiratory rate 20, pulse rate 64, and temperature 98.6 F. He was lethargic but oriented as to time, place, and person. The neck was stiff. There was a healed scar over the left mastoid area. The left eardrum was thickened but showed no evidence of active infection. The scalp at the site of application of the tongs was healed. There was a right hemiparesis with exaggerated deep tendon reflexes and an extensor plantar response.

The hemoglobin was 15.4 gm. and the white blood count was 6,700 per cubic millimeter. Roentgenograms of the skull showed a radiolucent area in the posterior portion of each parietal bone. Roentgenograms of the cervical spine showed good alignment of the vertebrae and an old fracture through the lamina of the fifth cervical vertebra.

A lumbar puncture was done. The CSF pressure was 200 mm. water, and the cell count was 426 cubic millimeter, 95% of which were lymphocytes. Culture of the spinal fluid yielded no bacterial growth. A left carotid arteriogram was obtained and showed a shift of the left anterior cerebral artery to the opposite side and a downward displacement of the left middle cerebral artery.

A left parietal craniotomy was performed and a defect in the bone was found at the site of insertion of the tongs. The dura mater was intact. An intracerebral abscess was excised beneath the site of insertion of the tongs. Hemolytic S. aureus was cultured from the pus. He made a complete recovery.

One month later a craniectomy was performed on the right side with the removal of bone around the site of insertion of the tongs. This was done as a prophylactic measure, and culture of the excised bone was negative.

CASE 3.—A 45-year-old man was in an automobile accident and received a fracture-dislocation of the second cervical vertebra, multiple rib fractures, and a penetrating wound of the larynx with fracture of the thyroid cartilages. A tracheotomy was done and the laryngeal wound closed after admission to another hospital. The patient complained of pain in his neck on the day after admission. Roentgenograms of the cervical spine showed a fracture-dislocation of the second cervical vertebra. The neurologic examination at this time was said to have been unremarkable. Crutchfield tongs were inserted in the skull, and a satisfactory reduction of the dislocation was obtained. The tongs slipped out three times during the following two weeks. During this period, he developed a cellulitis about the insertion of the tongs. He was treated with chloramphenicol, but the scalp infection became worse. He developed spiking fever up to 101 F. One month after the accident, he developed a right hemiplegia. A diagnosis of brain abscess was suspected, and for this reason the patient was transferred to our care.

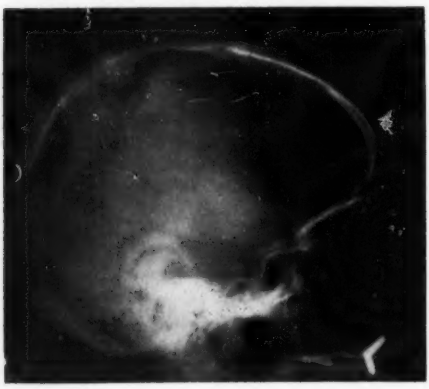
Examination: The blood pressure was 108/70, respiratory rate 36, pulse rate 66, and temperature 101.6 F. The Crutchfield tongs were still attached to the skull. There was a cellulitis of the scalp around the site of each tong insertion, and pus was draining from both wounds. A tracheostomy tube was in place. The patient was lethargic and disoriented with respect to location. He would respond to simple oral commands. He could not speak above a whisper because of the laryngeal injury. There was nuchal rigidity. There was a right hemiplegia with spasticity, exaggerated deep tendon reflexes, and an extensor plantar response. The abdominal response was absent on the right side.

The admission hemoglobin was 12.6 gm., and the WBC was 11,400. The urine was normal. Roentgenograms of the skull (Fig. 2) showed a radiolucent area in each parietal bone corresponding to the site of insertion of the tongs. Roentgenograms of the cervical spine showed good alignment of the vertebrae and a fracture through the pedicles of the second cervical vertebra.

When the tongs were removed, it was noted that the points had penetrated the inner table of the skull. A left carotid arteriogram was done and showed a shift of the left anterior cerebral artery to the opposite side and a downward displacement of the left middle cerebral artery. A left parietal craniotomy was performed. There was a tract consisting of granulation tissue connecting the dura at the tong site to an intracerebral abscess. The tract and abscess were excised. Hemolytic S. aureus was isolated from cultures of the pus from both the scalp wounds and the brain abscess. The organism was sensitive to oleandomycin (Matromycin), kanamycin sulfate (Kantrex), and ristocetin. A craniectomy was then performed on the right side with the removal of the involved bone. Culture of the bone chips from this side also yielded hemolytic S. aureus.

He made a slow recovery, with some residual paralysis in the right arm. The scalp wounds healed, and roentgenograms of the skull made two months after operation showed no further infection.

Fig. 2.—Lateral roentgenogram of skull showing osteomyelitis around site of insertion of tongs.



Comment

The surgical technique involved in the insertion of skull traction is well known to those who treat injuries of the cervical spine. In order to prevent such serious complications as reported here, the following points are emphasized:

1. The tongs should be replaced at a new site if penetration of the inner table of the skull occurs.

2. The tongs should also be replaced at a new site if they slip out of the skull at any time during treatment.

3. The tong device should be replaced by another method of cervical spine stabilization if infection occurs.

4. Antibiotics are important adjuncts to treatment but do not assure complete protection against infection.

Summary

Two cases of brain abscess and one case of fatal osteomyelitis of the skull are reported. These infections followed the use of tong traction to the skull in treatment of fracture-dislocations of the cervical vertebrae.

Duke University Medical Center, Box 3068.

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2. Crutchfield, W. G.: Further Observations on the Treatment of Fracture Dislocations of the Cervical Spine with Skeletal Traction, Surg. Gynec. & Obst. 63:513-517 (Oct.) 1936.

Continued Complaints Following Cholecystectomy *

C. ALLEN WALL, M.D., and THADDEUS J. WHALEN, M.D., San Francisco

The causes of continued upper abdominal complaints following cholecystectomy are illustrated in this exhibit. An understanding of the normal biliary mechanism and the physiologic alteration with disease facilitates the surgical approach to biliary tract disease. It is apparent that radiography, both preoperatively and on the operating table, plays a vital role in diagnosis.

Physiology

Bile is secreted by the liver cells at a maximum pressure of 300 mm. of water. As the sphincter of Oddi is normally closed, hepatic bile passes into the gallbladder, where it is concentrated and stored. Water and salts are absorbed by the gallbladder wall, and a small amount of mucin is secreted. The normal gallbladder, because of its distensibility, acts as a safety valve against elevated intraductal pressure. The kinetics of the entire biliary tract depend upon the bile flow control of the sphincter of Oddi and the "pressure bulb" function of the gallbladder (Fig. 1).

The gallbladder evacuates in response to a stimulus, particularly a fat meal. Fat, partially digested protein, or a high degree of acidity stimulates the cells of the duodenal mucosa to produce the hormone cholecystokinin. On liberation into the blood stream, cholecystokinin is transported to the gallbladder, causing it to contract. When the gallbladder contracts, relaxation of the sphincter of Oddi ensues and bile flows freely into the intestine. The sphincter of Oddi is also influenced by the autonomic nervous system (Fig. 2).

In disease states confined to the gallbladder, e. g., cystic duct occlusion by inflammation or calculus, control of biliary kinetics is transferred to the sphincter of Oddi. Relaxation of the sphincter occurs, allowing continuous escape of bile into the intestine. This biliary "incontinence," even during fasting states, prevents an elevation of intraductal pressures. The common duct remains normal in size. The sphincter of

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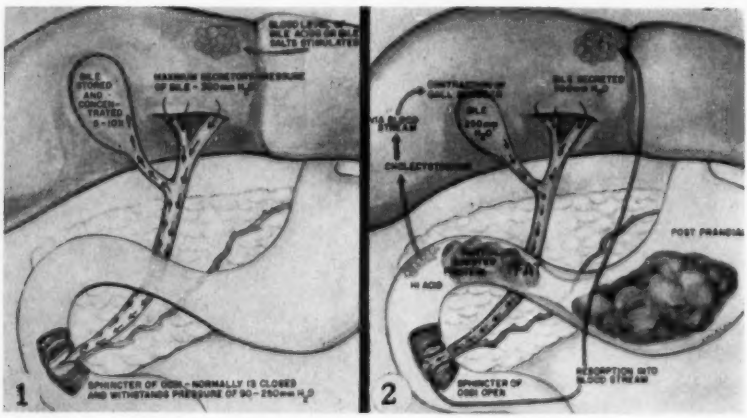
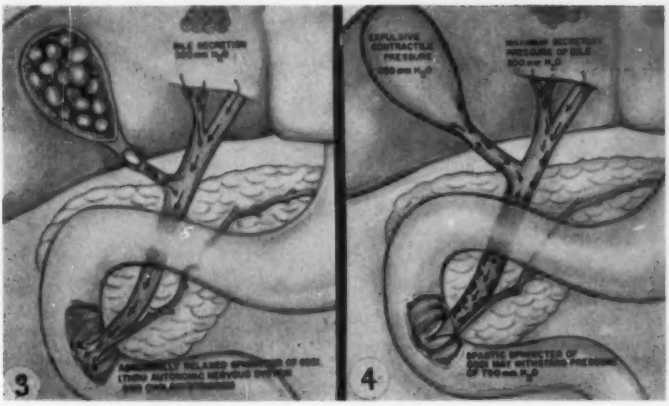
Department of Surgery, Saint Mary's Hospital.

* Surgery Illustrated. Shown as a scientific exhibit of the Section on Surgery, General and Abdominal, at the 107th Annual Meeting of the American Medical Association, San Francisco, June 23-27, 1958.





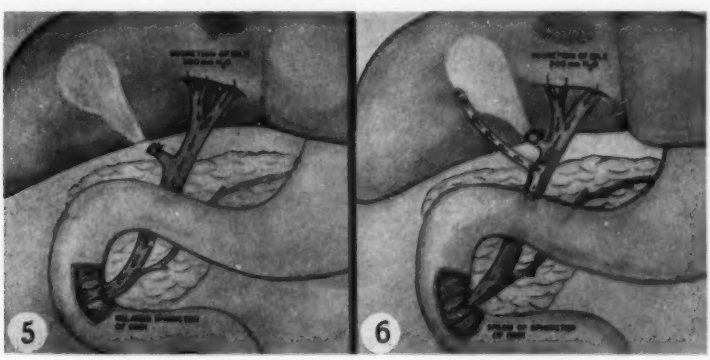
Oddi is under the influence of both cholecystokinin and the autonomic nervous system (Fig. 3).

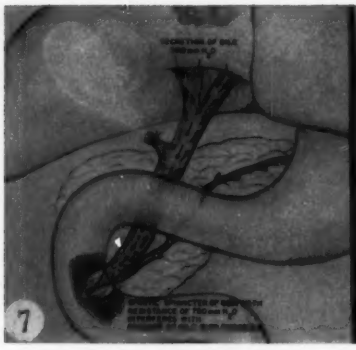
Under abnormal conditions, e. g., inflammation of the ampulla, the sphincter of Oddi may remain closed in a severe state of spasm and be capable of withstanding pressures as high as 750 mm. of water. With this resistance considerably higher than either the contractile force of the gallbladder or the secretory pressure of the liver, bile is prevented from entering the intestine. The gallbladder serves as a "buffer" mechanism against an elevated intrabiliary pressure by concentrating and storing the bile until relaxation of the sphincter occurs. Common duct dilatation may ensue (Fig. 4).

After cholecystectomy for disease confined to the gallbladder, "incontinence" of the biliary ducts develops with relaxation of the sphincter of Oddi. Dilatation of the bile passages frequently occurs. During the early postoperative phase there is continuous escape of bile into the intestine. Following a period of adjustment, some intermittency of bile flow into the duodenum may ensue (Fig. 5).

Following common duct exploration, additional alteration in biliary kinetics occurs. With excessive manipulation about the ampulla, e. g., Bakes dilators, the constrictor tone of the sphincter is increased by the surgical trauma. A "spastic" sphincter may ensue. Decompression of the common duct with a T-tube prevents an elevated intraductal pressure permitting external drainage of bile. Premature removal of the T-tube is followed by increased pressure within the biliary tree (Fig. 6).

Removal of a functioning, acalculous gallbladder in the patient with biliary tract symptoms whose disease is due to a spastic sphincter of Oddi will serve only to aggra-





vate the symptoms. The gallbladder functioned as a reservoir to relieve the excess biliary pressure by concentrating and storing the bile until such time as sphincter relaxation permits drainage into the duodenum. Removing this buffer mechanism will result in elevated intraductal pressure with dilatation of the biliary tree. Reflux of bile into the pancreatic duct may ensue. Backflow of bile into the liver occurs (Fig. 7).

In the patient with a hypertrophied sphincter of Oddi from spasm, destroying the function of the sphincter by sphincterotomy will permit continuous drainage of hepatic bile into the duodenum. Intrabiliary pressure will be reduced and some diminution in size of the ducts will occur. The gallbladder, even when normal, serves no useful function after sphincterotomy and should be removed. Some tonus at the ampulla may remain after sphincterotomy from contraction of the duodenal wall (Fig. 8).

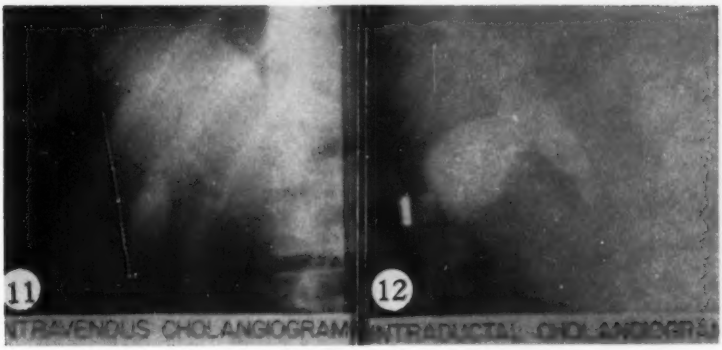
Radiographic Diagnosis

A flat film of the right upper quadrant may disclose radiopaque stones or air within the bile ducts from a biliary-enteric fistula (Fig. 9).

Oral cholecystography is useful not only to detect stones but also as an index of gallbladder function as judged by the degree of contraction following a fatty meal. A patent cystic duct is required for visualization (Fig. 10).

The intravenous cholangiogram with iodipamide sodium (Cholografin) will demonstrate the extrahepatic bile ducts as well as the gallbladder. Concentration of the media within the biliary system, dependent upon the excretory function of the liver, is impaired with hepatic disease (Fig. 11).

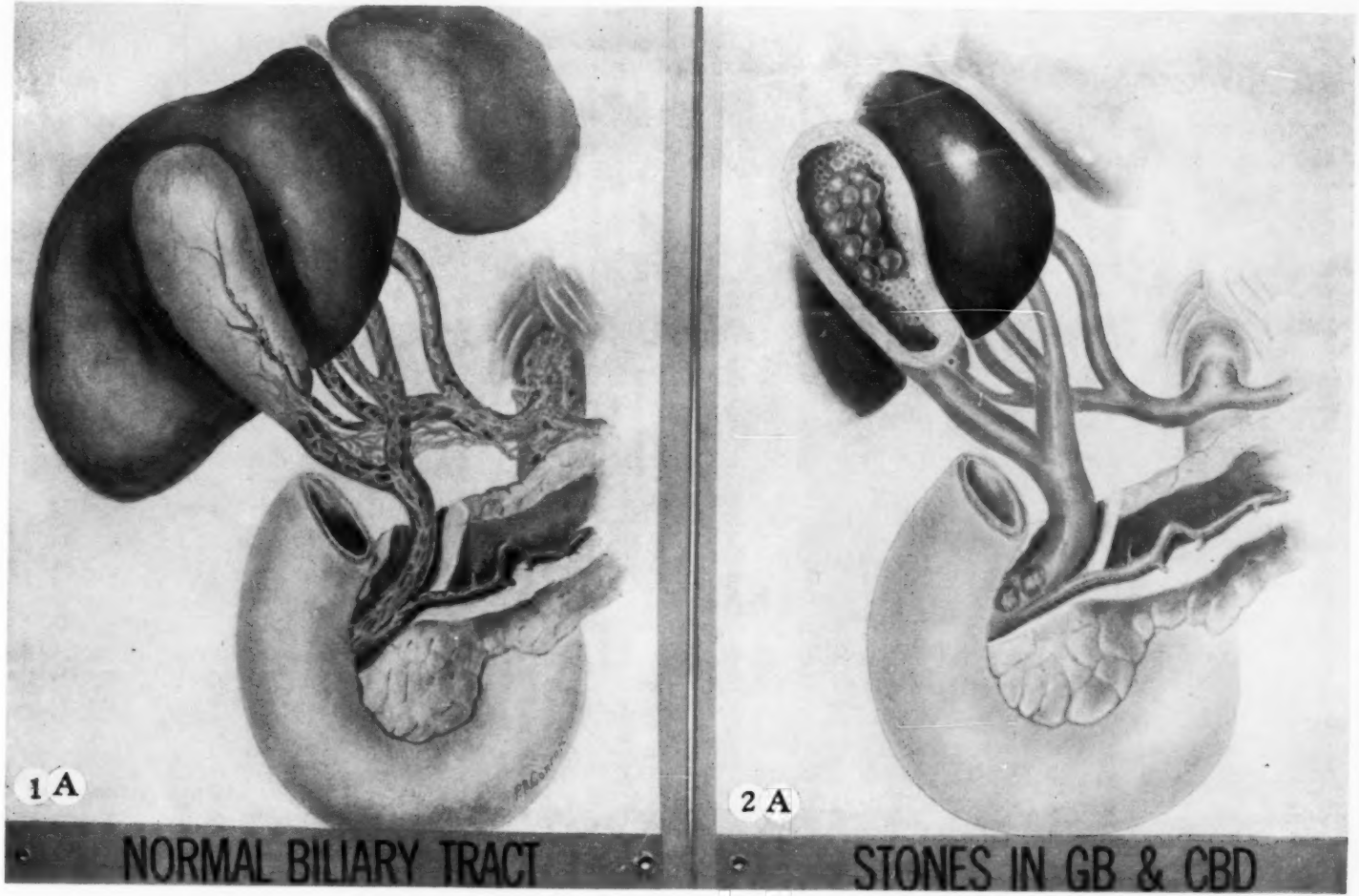
An intraductal cholangiogram may be performed on the operating table (operative cholangiography) or, after choledochostomy, postoperatively through the T-tube (delayed cholangiography) (Fig. 12).

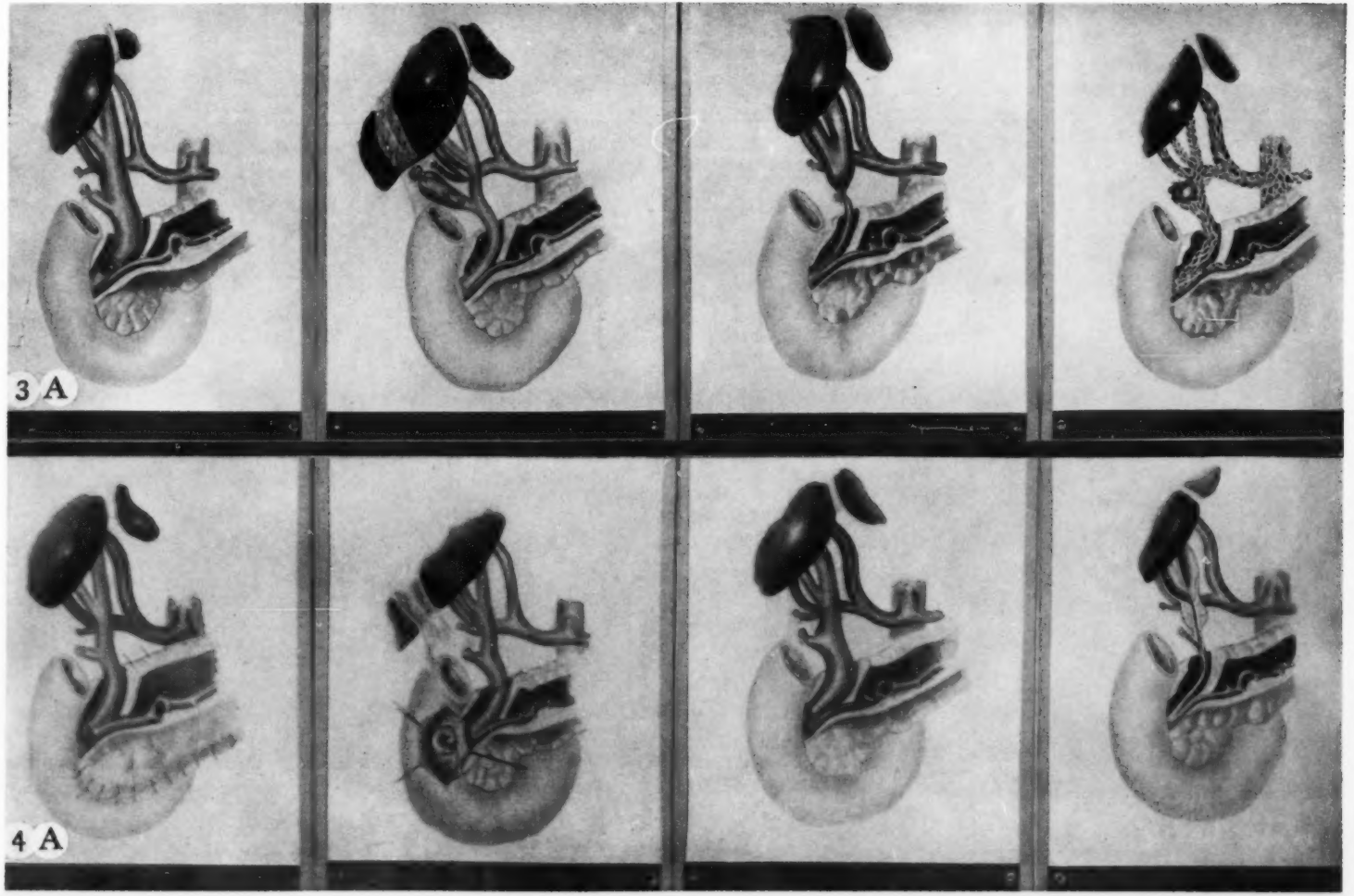


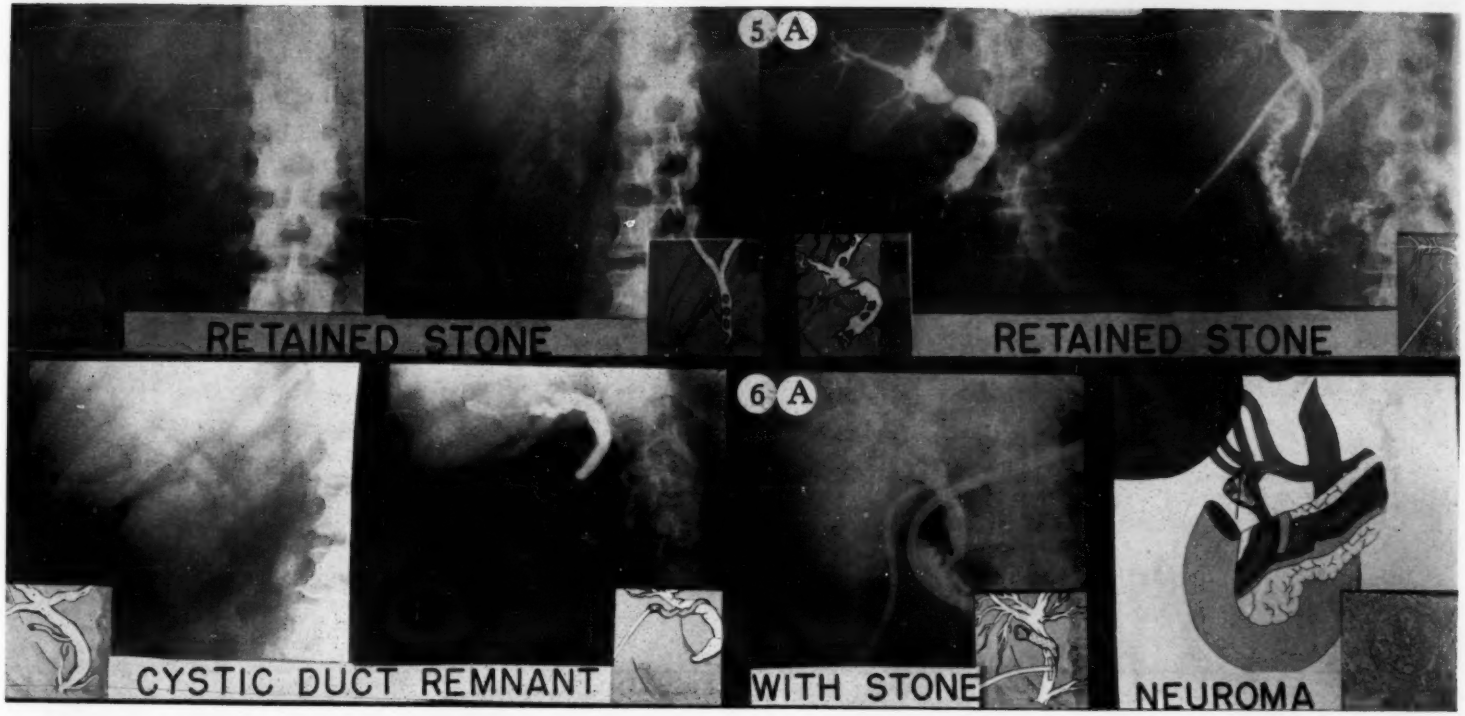
Postcholecystectomy Complaints

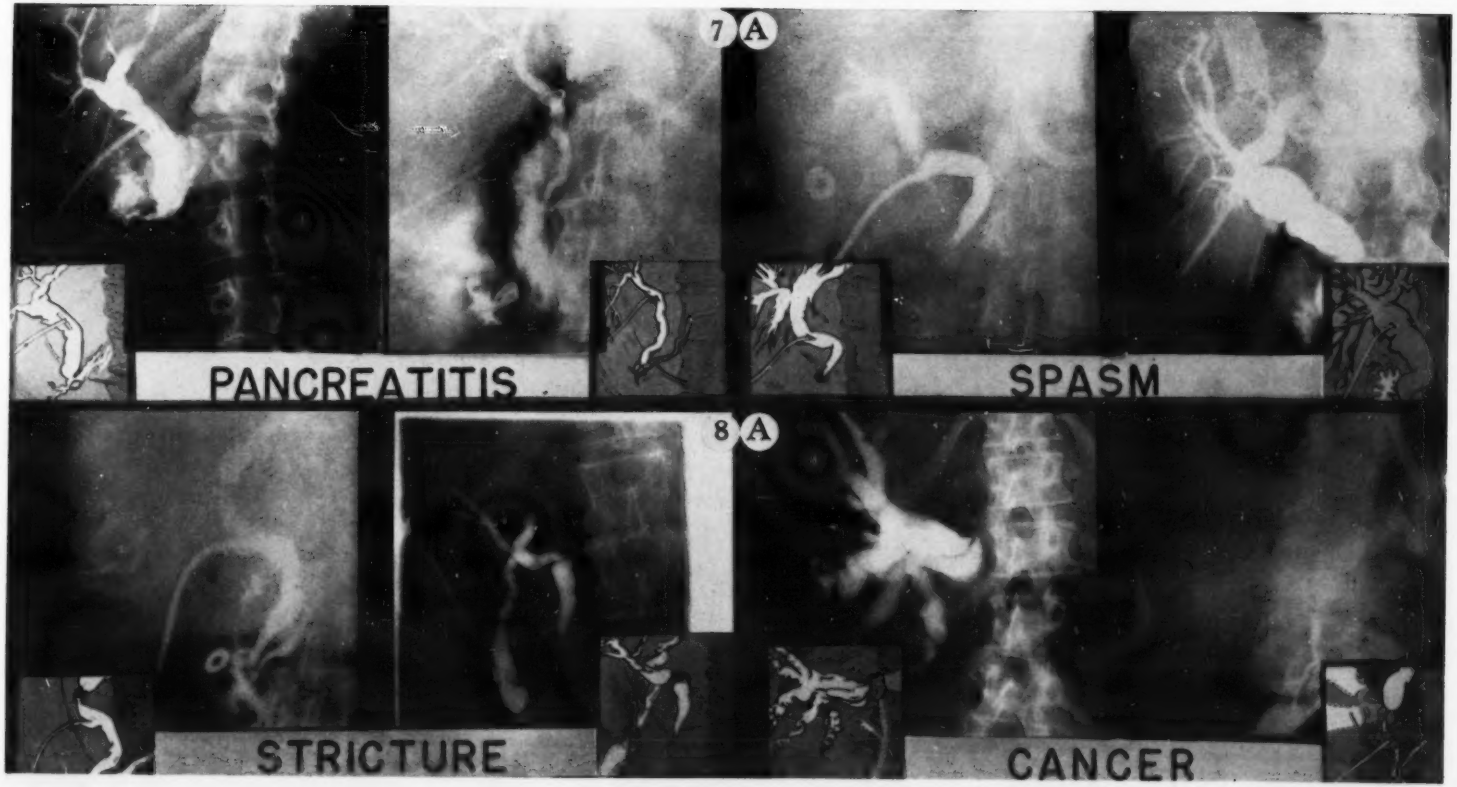
Cause	X-ray Diagnosis	Surgical Management
Retained common duct stone	Intravenous cholangiogram Operative cholangiography Delayed cholangiography	Explore common duct and remove stones
Recurrent pancreatitis Due to Fibrosis or spasm of sphincter of Oddi Common or pancreatic duct stone	Intravenous cholangiogram Operative cholangiography Operative pancreatography	Explore common duct Sphincterotomy
Bile duct stricture	Intravenous cholangiogram Operative cholangiography	Explore ducts and repair stricture
Cystic duct remnant	Intravenous cholangiogram Operative cholangiography	Resect redundant cystic duct
Neuroma of cystic artery and/or duct		Resect neuroma
Tumor	Intravenous cholangiogram Operative cholangiography	Decompress biliary system Resect tumor if operable

2020 Hayes St.


1 A
NORMAL BILIARY TRACT
2 A
STONES IN GB & CBD


3 A
4 A


5 A
RETAINED STONE
RETAINED STONE
6 A
CYSTIC DUCT REMNANT
WITH STONE
NEUROMA


7 A
PANCREATITIS
SPASM
8 A
STRICTURE
CANCER

U. S. Naval Medical Research Laboratory, U. S. Naval Submarine Base

CAPT. JOSEPH VOGEL (MC), U. S. N.

Foreword

In October, 1958, the members of the Advisory Panel on Medical Sciences, Research and Engineering, Office of the Assistant Secretary of Defense, visited the Naval Medical Research Laboratory at the U. S. Naval Submarine Base to hear a report by workers in the Naval Medical Research Laboratory and their problems peculiar to shipboard submarine and diving medicine.

Members of the panel were impressed with the methods used to attain these objectives, the facilities available, the accomplishment of these objectives, and the practical application of results of the multitudinous researches being carried out.

The problems which the medical specialists there have encountered were of sufficient general interest to all practitioners of medicine to warrant a report on them from Capt. Joseph Vogel, officer in charge of the laboratory. Captain Vogel agreed to write such a report. In addition to hearing reports of the work which is herein presented, members of the Advisory Panel took part in tours, including the diving tour, in the course of which demonstrations were given. A day's cruise on the U. S. S. *Nautilus* under the water of Long Island Sound gave members of the panel the opportunity to study various aspects of confinement within the submarine while the craft was in operation.

Submitted for publication May 1, 1959.

Officer in Charge, U. S. Naval Medical Research Laboratory, New London, Conn.

Fig. 1.—Captain Anderson giving a report of the polar expedition.

A photograph of members of the panel topside of the U. S. S. *Nautilus* also seemed worthy of publication, together with another of Captain Anderson giving a report of the polar expedition.

WALTMAN WALTERS, M.D.

Fig. 2.—Members of the Advisory Panel on Medical Sciences.

Left to right: Capt. Joseph Vogel (MC), U. S. N., Officer-in-Charge, Naval Medical Research Laboratory, U. S. Naval Submarine Base, New London, Conn.; Dr. Richard E. Bolt, Director of Acoustics Laboratory, Massachusetts Institute of Technology, Cambridge, Mass.; Dr. Donald W. Hastings, Professor of Psychiatry and Neurology, Medical School, University of Minnesota, Minneapolis; Capt. Oscar Schneider (MC), U. S. N., Secretary, Office of Director of Defense Research and Engineering, Washington, D. C.; Dr. Harwood S. Belding, Professor of Environmental Physiology, University of Pittsburgh, School of Public Health, Pittsburgh; Dr. John B. Youmans, Technical Director of Research, Office of the Surgeon General, Department of the Army, Washington, D. C.; Dr. Waltman Walters, Professor of Surgery, Mayo Foundation, University of Minnesota, Rochester, Minn.; Dr. Christian J. Lambertsen, Professor of Pharmacology, School of Medicine, University of Pennsylvania, Philadelphia; Dr. R. Keith Cannan, Chairman, Division of Medical Sciences, National Research Council, Washington, D. C.; Dr. Herbert Pollack, Associate Professor of Clinical Medicine, New York University Post-Graduate School of Medicine, New York; Dr. Richard A. Kern, Emeritus Professor of Medicine, Temple University Hospital, Philadelphia; Dr. Gioacchino Failla, Professor of Radiology and Director of Laboratory, College of Physicians and Surgeons, Columbia University, New York; Dr. Harold G. Scheie, Professor of Ophthalmology, University of Pennsylvania, Philadelphia; Wg. Comdr. J. C. Wickett, Staff Officer, Medical Services (Air) Canadian Joint Staff, Washington, D. C.; Dr. Maynard K. Hine, Dean, School of Dentistry, Indiana University, Indianapolis; Dr. Frank Hartman, Research Adviser, Directorate of Professional Services, Office of the Surgeon General, Department of the Air Force, Washington, D. C.; Grp. Capt. J. S. Howitt, Staff Officer Medical, British Joint Services Mission (AFS) Washington, D. C.; Dr. Truman Blocker, Professor of Surgery (Plastic and Maxillofacial) Department of Surgery, University of Texas Medical Branch, Galveston, Texas; Col. Richard L. Marks, Army Staff, British Joint Services Mission, Washington, D. C.

The objective of the Naval Medical Research Laboratory is to conduct medical research on problems peculiar to shipboard, submarine, and diving medicine, and to train personnel of the Medical Department for duty with the Submarine Force. An elaboration of this mission in local organizational plans states that the laboratory is responsible for "augmenting the effectiveness of the Submarine Force by research and development, and by the application of the findings to the objectives of personnel operations."

Functions

Research.—Investigation is carried out on projects which have been officially approved and for which funds have been allocated by the Bureau of Medicine and Surgery. In the pursuit of these projects, the laboratory maintains close liaison with the National Academy of Science, the National Research Council, the Office of Naval Research and other government research laboratories, bureaus, and agencies, as well as with universities, colleges, and civilian laboratories.

Examination and Assessment of Volunteers for Duty with the Submarine Force.—The laboratory conducts the physical, psychiatric, and psychologic examinations of all volunteer applicants for the Submarine School, to determine fitness for submarine duty in accordance with current standards.

Training.—Postgraduate training in submarine medicine is given to naval medical officers. Additionally, the laboratory conducts a course of medical training for hospital corpsmen entering submarine service, and a special training course in radiologic health for corpsmen preparing for duty with nuclear-powered submarines.

The laboratory provides medical and technical services for the Submarine Escape Training Tank, and advises and assists in the prevention and treatment of casualties in the course of this training. This will be enlarged upon later. A submarine medical officer from the laboratory staff participates in and is present whenever training in individual submarine escape is given.

An additional service is rendered to diving personnel of submarine rescue vessels by mixing and maintaining sufficient amounts of gas mixtures for routine and emergency deep diving.

Historical Aspects

The laboratory was established in 1942. Mobilization and subsequent expansion of the Submarine Force resulted in a need for a more efficient, accurate determination of physical and psychologic standards peculiar to the demands of the Submarine Force, the establishment of reliable, fast methods of assessment for screening volunteers, scientific methods for the selection of sonar operators, studies in day, night, and color vision, and the application of these factors in the selection and training of effective lookouts. Until Feb. 23, 1944, the laboratory was conducted as a unit of the dispensary of the Submarine Base, and on that date it was made a separate department of the Submarine Base. This organizational form continued until June 30, 1946, when the Secretary of the Navy established the laboratory as a separate activity under the management and technical control of the Bureau of Medicine and Surgery.

To the original branches of the laboratory devoted to research in assessment of personnel, vision, and hearing have been added physiology, human engineering, and dental branches. From the quarters of two rooms in the basement of the dispensary initially occupied, the laboratory is now housed in four buildings. The physiology, sound, and dental branches recently have been moved to a building specifically modified to their needs. The dedication of this building coincided with the First International Symposium on Submarine and Space Medicine held at the Submarine Base the week of Sept. 8 through 12, 1958.

The laboratory has additional space at the building of the Escape Training Tank for experimental work and the testing of human volunteers in physiology. This room con-

tains a recompression chamber as well as other laboratory equipment.

Personnel

The laboratory staff is composed of approximately 100 persons. At this writing there are 50 civil service employees and 45 military personnel: 16 officers and 29 enlisted technicians.

Training

Rapid expansion of the nuclear-powered submarine fleet, coupled with the decision by the Naval Reactors Branch of the Bureau of Ships to assign a submarine medical officer aboard each such submarine for at least a year, resulted in a concentrated effort to recruit these medical officers and to condense their training time. Pioneers in this group assigned to U. S. S. *Nautilus, Seawolf, Skate,* and other recently commissioned submarines were given a broad, comprehensive training which included a year of work in radiobiology at either Reed College or the University of Rochester, a special course under the auspices of the Armed Forces Special Weapons Project, six months at a reactor site in Arco, Idaho, or West Milton, N. Y., added to the regular six-month course in submarine medicine at the Submarine Base, New London, Conn., and the Deep Sea Diving School, Naval Gun Factory, Washington, D. C. The rapidity with which new submarines are coming down the ways has forced a revision of this lengthy training period, resulting in a "streamlined" six-month training program sufficient to qualify a medical officer for this type of duty. The longer course is still available, but assignment to it is based on the personnel needs of the service.

Medical-officer volunteers selected for training in submarine medicine report to the U. S. Naval Submarine School at New London as part of the regular line-officer student class. For six weeks they receive instruction, with their line-officer classmates, on the construction and operation of a modern submarine. The line officer continues his course at the Submarine School on the finer points of the submarine navy to learn proficiency in the operation of a submarine. The medical officer comes to the laboratory, where his education as a submarine medical officer begins. Courses in habitability, ventilation, human engineering, Navy regulations, Navy correspondence and filing, procurement and fiscal procedures, submarine dentistry, psychiatry, preventive medicine and industrial hygiene, otolaryngology, physiology of vision, gases, metabolism, environment, assessment of personnel, radiologic health, visual engineering and psychophysiology, and medical department administration are given, totaling approximately 300 hours. Guest lecturers, who are authorities in some of the fields covered, assist instructors from the laboratory in presenting these courses to the prospective submarine medical officer.

The demands placed on the Training Division of the Medical Research Laboratory in all its phases have been markedly increased by the nuclear-powered submarine program. Not only has a new section for training hospital corpsmen and medical officers in radiobiology been established, but student input in all categories has increased by a third. Added to this was a radical change, adopted as standard in 1956, in the method taught for making individual escape at the Escape Training Tank. This meant that the entire Submarine Force had to be retrained in this method in addition to the number normally trained prior to entrance into the Submarine School.

A brief explanation of submarine escape follows for those readers unfamiliar with the function of the Submarine Escape Training Tank (Figs. 1 and 2).

The Submarine Escape Training Tank.— A submarine medical officer from the staff of the laboratory is present whenever pressure tests or training sessions in the Tank are given. Every volunteer for the Submarine Service must demonstrate his ability to equalize pressure to a simulated depth of 112 ft. in the recompression

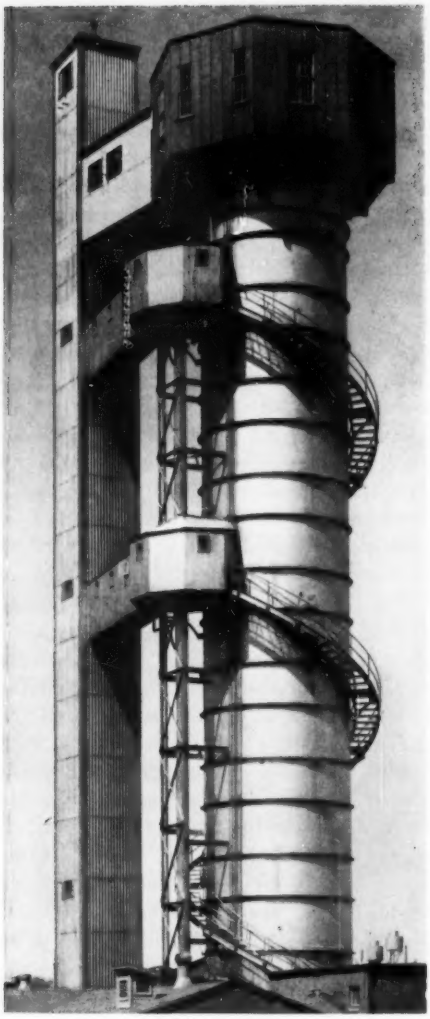


Figure 1

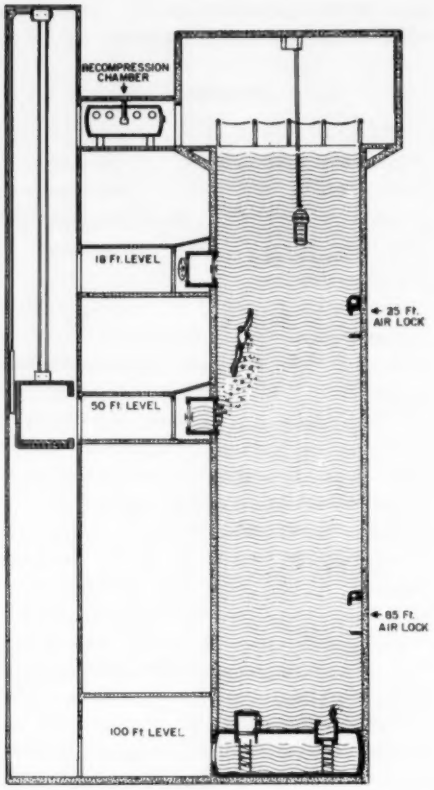


Figure 2

Fig. 1.—The Submarine Escape Training Tank of the U. S. Naval Medical Research Laboratory, Submarine Base, New London, Conn.

Fig. 2.—Schematic arrangement of the interior of the Submarine Escape Training Tank. Escape from this tank at depths of 50 ft. or less is part of required training; escapes from the depth of 100 ft. are voluntary on the part of the trainee.

chamber (50 lb. per square inch gauge) and successfully ascend from depths up to 50 ft. in the Escape Training Tank. Escapes from the 100-ft. level are voluntary.

This training device serves a dual purpose. Not only does it give a submariner the confidence and ability to escape from a disabled submarine unable to surface, but it is an important screening device in the assessment program. Escape training represents a very real situation of stress to which those temperamentally unsuitable candidates for the Submarine Service react revealingly. Borderline claustrophobes and others with personality traits which would militate against their successful adaptation to submarine life and who have not been disqualified by means of usual assessment procedures are eliminated by this procedure.

Escapes with a rebreathing bag, the submarine escape appliance (S. E. A.), or Momsen lung, was standard practice prior to the present method of escape training known as the "buoyant ascent" or "blow-

and-go" method. With the aid of an inflated life jacket to assure positive buoyancy, the submariner steps out of the lock which has been partially flooded to equalize the pressure in the escape lock to that of the water of the Tank itself above it. Having inhaled deeply in the lock just prior to this, he exhales forcibly, then is given a signal to ascend by an instructor, and starts on his way to the surface, exhaling continuously all the way up. This, of course, is possible as a result of the pressure of the residual air in his lungs, which is equivalent to the pressure of the air breathed under pressure in the lock. As he ascends, with the pressure decreasing, the volume constantly increases in accordance with Boyle's law. If he should fail to exhale continuously or sufficiently enough to vent this excess volume of gas built up during the ascent, or if some pulmonary pathologic process "traps" this air, as may occur in certain emphysematous or anomalous conditions in the pulmonary fields, rupture of the pulmonary tissue would ensue, resulting in air embolism with serious and occasionally fatal outcomes. Every precaution is taken to prevent such accidents, including the making of a 14- by 17-in. roentgenogram of the thorax prior to escape training, careful instruction in the correct method of escape, an explanation of the reasons therefor, as well as very close observation by the instructors and the submarine medical officer, who are in the water with and who follow each escapee closely. If at any time it is seen that the escapee is not exhaling or that he is exhaling insufficiently, he is immediately stopped by an instructor and taken into the nearest air lock.

At the top of the Tank, a few steps from the water, there is a recompression chamber. Casualties are brought to this chamber, accompanied by the submarine medical officer and a tender; then recompression to an equivalent depth of 165 ft. is accomplished in less than a minute. Treatment is carried out in accordance with standard Navy procedure for conditions of this type. In the past two years there have been two casualties successfully treated, and one death. In the latter case a massive air embolism developed as a result of air trapped in the lungs by a broncholith. This case, with another involving a casualty which happened as a result of air trapping, has been described in a report by Liebow, Stark, Schaefer, and me, published in the *Armed Forces Medical Journal* in March.[1] Fatalities have occurred at a rate of less than 1 in 10,000 ascents. A total of 66 casualties and 8 fatalities have resulted from 250,000 ascents, the total number of ascents attained approximately a year ago.

Physiologic research in which instructors of the Escape Training Tank serve as volunteers has been valuable in studies of adaptation to carbon dioxide. Casualties have added to our knowledge of the mechanism for the development of air embolism, as well as the problem of trapped air in the pulmonary tree and the role of this condition in the production of air embolism.

Personnel Examination Division

The Personnel Examination Division is concerned primarily with screening candidates, both enlisted men and officers, for admission to the U. S. Naval Submarine School. The physical and psychologic standards are set up by the Bureau of Medicine and Surgery and the Bureau of Naval Personnel.

Although a preliminary physical examination of the volunteers is done in the field on initial application of the candidate, this procedure is repeated at the laboratory with other specialized examinations, including a battery of psychologic tests and audiometry. This situation, whereby large numbers of subjects are available for new testing procedures, affords the assessment branch excellent opportunities for assessment research.

Close liaison on the part of the laboratory with the operating submarine forces has made it possible to recommend certain changes in physical standards compatible with efficient operation. As a result of the

increasing submergence capabilities of the nuclear-powered submarine, recommendations have been made for certain changes in visual standards. The submarine has become more and more dependent on its "ears" for many functions formerly accomplished visually.

Research Division

The six branches of the Research Division form a well-rounded and versatile group, enabling the laboratory to produce the results called for by its mission. To assist in the coordination and guidance of these efforts, the over-all supervisory position of scientific director was created in 1957. The laboratory was extremely fortunate in obtaining the services of Dr. Walter R. Miles as the first incumbent for this position. Dr. Miles is a distinguished psychophysiologist with an excellent background. More recently he served as professor of psychology in the Yale University School of Medicine from 1931 to 1953, and then worked for the Turkish Government in setting up a department of experimental psychology at the University in Istanbul. He has been with this laboratory slightly more than a year, and will afford a source of stability and continuity in the research program, which operates under the military supervision of a naval officer who, of necessity, rotates to new duty every few years.

Dental Branch.—The head of the Dental Branch is Capt. W. R. Stanmeyer (DC), U. S. N., who has had wide experience in dental research. Briefly, the program of this branch is devoted to studies on the following:

1. Effect of stresses of submarine service on oral health

2. Effect of carbon dioxide on the calcification of dentine

3. Effect of exposure to and withdrawal from atmospheric contaminants

4. Effect of stress (atmospheric contaminants, high noise levels, and the like) on cariogenic activity

5. Effect of stress (atmospheric contaminants, high noise levels, etc.) on tissue repair

6. A study of oral health in Antarctica This study is concerned with the men who for 12- to 18-month periods have been or will be living almost completely isolated from the rest of the world in several bases in Antarctica. The several operations are considered unique in view of their prolonged nature, the lack of physical contact with the outside world during the long Antarctic winter, the restrictions on communication, and in general the extreme conditions of stress to which the men are subjected in the high winds and constant low temperatures. The dental program consists of clinical examinations, field observations, and careful histories of all personnel with and without symptoms. It includes studies of the pathologic aspects of extracted teeth and certain features of oral health, such as (1) the incidence of caries in relation to diet, oral hygiene, and stress; (2) changes in oral flora, and (3) the relationship of psychosomatic factors to dental complaints. Other phases of the program are involved with the testing of rubber protective devices to insulate the teeth, and a study of the performance of various dental fillings from the standpoint of insulation, retention, and discoloration. Elective phases of the program include studies of changes in the pH of dental plaques after a carbohydrate rinse in relation to a cold environment and the collection and preservation of saliva for future studies on electrolytes. Data from the studies outlined above are in the process of statistical analysis at the Medical Research Laboratory.

Another phase of this study includes the close clinical and radiographic observance of oral conditions of persons living in Antarctica correlated with complete cellular and biochemical studies of month-by-month changes occurring in their blood. Collected data will be returned to this country in May, 1959.

Auditory Research Branch.—This branch, devoted to research in sound, is headed by

Dr. J. Donald Harris. Dr. Harris is a doctor of philosophy in physiologic psychology, with many years of experience in this type of research.

Four major sections constitute the branch: Audiology, Psycho-Acoustics, Sonarman Performance, and Bio-Acoustics.

Sonarman Performance Section: The problem of selection of sonarmen is concerned with persons aboard submarines assigned to the special listening gear known as "prosubmarine sonar." The sonarman's task is to listen as if his head were immersed in the water and to interpret whatever sounds may come to him. In this task he will use a dozen or more specific auditory abilities, such as discrimination of intensities, rhythms, frequencies, and timbres, contact detections, temporal patterning, recognition of targets, distinction between targets and many others—some primary auditory abilities, some rather complex.

There are two aspects to the problem of selection. One is the development of adequate criteria, or the ranking of active sonar operators on the basis of order of excellence, including the job analysis of such a task, and a second, the development of selection tests which can be understood and performed by persons who never have had any experience in sonar.

Five primary auditory abilities have been identified, two in the field of pitch discrimination and three in the field of loudness discrimination, and it is certain that a dozen more will exist in the fields of rhythm, time discrimination, masking, and contact detection.

It is expected that within a very few years the fundamental auditory abilities in the human being will be identified and will result in the formation of a small battery of tests to sample all these abilities. This battery of weighted tests, then, should serve for an indefinite period as a battery of tests in this sonar area, or indeed for any listening or communications job.

Psycho-Acoustic Section: This section has been developing the fields of pitch discrimination, intensity discrimination, auditory fatigue and adaptation, auditory tracking, and the relationship between the special senses of vision and audition in sensory display, in a broad effort to provide theoretic bases for the work of selection of sonarmen, and in an effort to provide maximally effective auditory displays for any man-machine system.

Audiology Section: This section is charged with administering the Bureau of Medicine and Surgery's hearing conservation program in this geographic area. This program involves measurement of noisy work spaces, identification of areas in which personnel need protection, specification and education in the use of protective devices such as earplugs and earmuffs, performance of monitoring audiometry on persons exposed to these areas of noise, and attempts at the devising of new audiologic tests to assist the otologist in the diagnosis of hearing disorders. In connection with this work, preparations are in progress to put into operation a sound-speech machine operating upon optic and mechanical principles which will create speech and speech-like sounds with the stroke of a white paint brush. This machine will be used for studies on speech communication under adverse or low-fidelity conditions, and will be used to create a wide variety of sounds in support of our general psycho-acoustic program.

Bio-Acoustic Section: This section is concerning itself at present with three major problems. First, the biochemistry of the production of electricity in the peripheral organ of hearing (when a sound strikes the ear, the ear itself creates a charge of electricity of as much as a millivolt before the first-order neuron is activated). This electricity can be used to study the peripheral organ as a consequence of changes in the physiology of the animal. For example, the respired gases may be changed; the level of blood sugar may be altered by the injection of insulin or by other means, and enzymes and enzyme inhibitors and poisons may be introduced either locally or sys-

temically. Such a program is aimed at understanding how hearing as a total process is affected by various environmental and metabolic changes. One interesting observation has been made recently, in that it has been determined that a considerable portion of the oxygenation of the high-frequency end of the cochlea may occur directly across the round window from the middle ear.

The second problem in the Bio-Acoustics Section is the study of the recovery of the potential of the ear and of the auditory nerve from intensities up to 140 db. at durations up to about a half-hour. The attempt here is to determine the strength-duration curve for the peripheral organ and for the first- or second-order neurons.

The third problem is the response of the auditory cortex of the cat to complex stimuli. Responses of the human ear to tone-in-tone and to tone-in-noise have been investigated with the Békésy audiometer technique. It is proposed to introduce these same tones into the ear of the cat and to pick off potentials from the auditory cortex with a four-electrode ray. The hope here is to provide some sort of a break-through between human psycho-acoustics and the auditory nervous system of the animal.

Vision Branch.—The Vision Branch is headed by Dr. Forrest L. Dimmick, who has had a long and successful career in the field of visual psychology research.

The work of the Vision Branch derives from four problems inherited from wartime studies, and has expanded with the evolution of the more complex military applications. The four original areas were those of visual selection, vision at low levels of illumination, and the testing of night vision and adaptation to dark.

Sensitivity to various colors is a problem arising out of the large and complicated signal panels and displays of cathode-ray tubes. Detection of signals and recognition of objects and coded information have raised problems of color discrimination for both normal and color-blind persons and specification of the discernible differences. Modern developments have necessitated human operation under extreme environmental conditions in space and submarines; these raise problems of the visual effects of various artificial atmospheres and of vision under water. An additional program of work concerns the evaluation of protective optical media for flight personnel.

Visual Selection: Visual selection was the subject of an extensive cooperative research project carried out under the auspices of the Office of the Adjutant General, U. S. Army, Washington, D. C. From this study it became apparent that checkerboard targets offer the best means for measuring visual acuity for purposes other than optometric or ophthalmologic examinations. To put the recommended targets into practical use required careful study of the techniques to obtain satisfactory targets and of the conditions under which to use them. A quick, simple test in which these targets are used has been devised for untrained persons and is now being evaluated.

Although size has been used as the standard measure of visual acuity, it has been recognized that discrimination of brightness is parallel to, if not another aspect of, discrimination of size. Procedures are being devised to make measurements that will give a more realistic picture of the change of visual acuity away from the "sharp" image of correct focus toward the blurred images of ametropia.

To provide an estimate of the visual acuity required to carry on various submarine jobs, a survey of all the visual tasks in a submarine was made. The resulting measurements have been analyzed, and from them we are able to determine the acuity required.

A complementary survey was made to determine the visual acuity actually present in a sizable group of submariners. Standard measurements of acuity were made among more than 1,000 men serving on submarines, and an analysis of those data was carried out. Among the questions raised and partly answered is the effect of service in the submarines on the visual acuity of the men.

Directly related to that is the question of whether certain visual aids, such as binoculars and periscopes, can correct refractive errors. It was shown that astigmatic errors cannot be corrected, and consequently were the most serious type of defect. Since at present the best method of diagnosing astigmatism is the time-consuming clinical examination, a simple means of screening men for astigmatism has been under study, and a test based on the findings of this investigation is in preparation.

Studies of the relationship of two measures of acuity, the Snellen letter chart and the Ortho-Rater, have been completed, and conversion factors found for translating one acuity score to the other.

Vision at Low Levels of Illumination: This second group of problems emanated from an experiment which was transferred to the laboratory by Dr. Franklin Burger, an ophthalmologist of Cambridge, Mass. He had carried out extensive testings to determine the nature of vision at low levels of illumination, with particular emphasis on visual acuity. However, the Navy was interested also in the question of vision at low-light levels as it applied to problems of the training of lookouts.

A successor to Burger's experiment was set up with a more carefully controlled set of conditions to enable us to measure acuity at very low levels of light. This obviously was directed at the problem of the acuity of lookouts at night. In connection with this same question, there had arisen in the literature much discussion about the possibility of improving night vision by the use of minus spherical lenses. The underlying bases for this "night myopia" are being investigated to determine to what extent it is based upon accommodation and thus how possible such corrections are.

It also became apparent that information on the sensitivity of the eye to various colors at low levels of illumination was lacking. Studies made of color vision at levels of light comparable to twilight and moonlight have shown which colors are most visible under these conditions, which should be viewed off center for best detection, and how to measure them when the illumination is below that at which ordinary light measures are applicable.

Examination of other factors, such as brightness-contrast, at low levels of illumination are under investigation. The adage that "in the dark, all cats look gray," is applicable to this type of visual problem, since a detection task at night is discernment of an object that looks gray against a gray background. The degree to which individual differences in the ability to see at night are affected by age and size of the pupil have been studied and are being analyzed.

Testing of Night Vision: The third project, transferred from Camp Lejeune, N. C., to New London, was the comparison of three tests of night vision which had been used during the Second World War.

Personnel Assessment Branch.—The staff of this branch is composed of two research psychologists who are doctors of philosophy, two Medical Service Corps psychologists, and three technicians. Dr. Benjamin B. Weybrew, head of this branch, has been with the laboratory for approximately six years, and he conducted much of the important research applicable to assessment for the Submarine Force.

The program of this branch may be divided into three somewhat overlapping areas: research on techniques of selection, research on motivation and group processes, and research on stress and fatigue.

Research on Techniques of Selection: Work in the area of selection technology has resulted in usefully valid selection cutoffs for enlisted men in the realm of verbal, mechanical, and arithmetical aptitudes. Educational achievement, pay grades, and scores on a psychiatric screening questionnaire (the personal inventory barometer, PIB, devised by the staff of this branch) combine to give predictive validity in the 0.50 to 0.60 range.

The problem of identifying "poor" psychiatric risks to be rejected for the Sub-

marine Service has been approached in several ways. First, a reasonably well-standardized interview by a submarine medical officer has been shown to have considerable validity in terms of predicting achievement level in Submarine School. Second, a group form of Murray's thematic apperception test, although not well-validated statistically, provides the interviewer with useful indicators of motivational conflict, deviant attitudes, and the like. Finally, by the use of factor analytic techniques, a number of psychomotor, perceptual, and personality tests and trait-ratings have been grouped, and the results suggest that the most valid predictors of success in the Submarine Service are related to verbal skills and traits of emotional stability and social effectiveness.

A slight change in the focus of the research in techniques of selection is planned in view of the need for fewer and more highly specialized men to comprise the crew of the missile-firing submarines. Currently, about 25% of the research effort is being directed toward the examination of the interrelationships of bodily states and behavior. In this connection, a recent pilot study examined the relationship of autonomic nervous system reactivity and ratings with respect to traits related to emotional stability and temperament. As indices of autonomic tone, changes and recoverability of palmar skin conductance during stress were employed. Results of this research suggested that the characteristic level of skin conductance, as well as the recoverability after stress, may be predictive of the ability to withstand the stresses of the pressure chamber and, in addition, seems to be correlated with certain temperamental traits. The next step will be to examine the predictive validity of these or similar autonomic indices with respect to adjustment criteria obtained during protracted submergence. These findings will be used as clues in collaborative research with the Physiology Branch of the laboratory, with employment of a climatized chamber (to be constructed shortly) as a means of obtaining data pertinent to the problem of the interaction of psychologic and physiologic variables as they are related to adaptability to the stressors of long submergence.

Motivational and Group Processes Research: Two problems are the main concern in the area of motivational research: (1) the problem of initial motivation to volunteer for submarines, and (2) the problem of maintenance of motivation after qualification for the Submarine Service. One study of the motivation of enlisted men to volunteer suggested that status motivation, symbolized by wearing of the coveted dolphins, opportunity for technologic training, and the additional pay for hazardous duty, in descending order of importance, are the three most significant motivational components related to volunteering. Another study in which the need structures of enlisted volunteers were compared with those of officer volunteers also was completed. Briefly, officers exceed enlisted men with respect to need for achievement and need to dominate. On the other hand, enlisted men exceed officers with respect to exhibitionistic needs and needs for abasement.

To date, no systematic study of the problem of motivational maintenance has been carried out other than the collection of data indicating when, during long submergences of the nuclear-powered submarines, motivation begins to diminish excessively.

A study designed to assess the initial motivation of officer volunteers was planned for January, 1959. In addition, a study designed to obtain data about officers and enlisted men which will be predictive of motivational intensity and persistence necessary for a person to revolunteer for successive long submergences demanded by the fleet ballistic missile (*Polaris*) program also is planned for 1959.

In the area of group processes research, two kinds of data have been collected. In the first place, observations made during leaderless discussion groups in the small-groups laboratory at the Medical Research

Laboratory have been shown to have considerable relationship to the achievement of success in the school of submarine medicine technique. Second, some data relevant to the changes in interpersonal relationships of the crew during long submergence suggest moderate increases in the frequency and intensity of negative interpersonal attitudes of the men under the conditions of long submergence. The focus of the work in the area of group processes research will be to attempt to assess the individual attitudinal structures which result in maximized cohesiveness of a submarine crew under conditions of long submergence. Both laboratory and operational studies are planned along these lines.

Stress and Fatigue Research: Three lines of research in this area have been followed in the past: (1) use of the recompression chamber and tank training as a stress situation; (2) employment of laboratory-contrived stress situations, and (3) use of the stressors of long submergence. Results of one study demonstrated substantial increases in the urinary output of 17-ketosteroids during tank training. Moreover, there is some evidence that past aquatic experience and the frequency and severity of neurotic traits are related to performance in the training tank and pressure chamber. In the laboratory, an exploratory study (1958) resulted in some indication that experimentally induced monotonous and repetitious activity results in lowered vigilance and, in some persons, a sizable imbalance of the autonomic nervous system. These findings, taken together, provide several hypotheses as to the possible mechanism or mechanisms by which the syndrome of fatigue occurs.

Stress studies during long submergence have been carried out aboard the *Nautilus* and *Seawolf*. At present, self-reported symptoms of fatigue rather than more objective measurements of autonomic and perceptual processes seem to be the most predictive of the length of time persons can adapt effectively to conditions of submergence.

Plans for the immediate future include explorations into the relationship of autonomic balance to performance and subjective symptomatology—all as a function of laboratory-contrived stress as well as a function of the operational stressors of long submergence. Three general research problems are to be examined by this research: (1) estimates of the maximal submerged time before fatigue, boredom, and other symptoms of debility arise; (2) factors contributing to, or predictive of, the individual differences in adaptability to stressors encountered during long submergence, and (3) methods of reducing the noxious and debilitating effects of protracted periods of submergence.

Human Engineering Branch.—This branch is headed by Lt. J. A. Moody (MSC), U. S. N. It is concerned with the application of scientifically derived information on human behavior to the design of components and systems for the achievement of maximal effectiveness in the operation and support of these in the field. The problem of habitability, especially as is relates to submarines, is preeminent in the work of this branch. The evaluation of new materials is an example of this work, as is lighting. The construction and use of automatic electronic computers to assist in the making of decisions by presenting firsthand the information necessary for this purpose is another area of this work.

The psychophysical problems of perception as related to form, depth, and movement constitute an important area of investigation by this branch.

As a result of these studies, a new dial design and new instrument design involving digits more conspicuous and legible under various operating conditions for use aboard submarines have been accepted for use.

Physiology Branch.—Dr. Karl Schaefer, head of the Physiology Branch, was educated in Germany and taught physiology at the University of Heidelberg. His service in the German navy in World War II was devoted largely to the physiologic ef-

fects of submergence on personnel serving in the submarine service. This experience has provided him with an excellent background for the pursuit of these and associated studies carried on in this branch at the Medical Research Laboratory. Dr. Schaefer has been appointed to the Armed Forces-NRM Committee on Bio-Astronautics.

Studies have been carried out in three fields.

Toxicity of Carbon Dioxide: The toxicity of carbon dioxide has been a cardinal problem in submarine medicine. Based on experiences in World War II, particularly on German submarines, the existing stated limits of tolerance to carbon dioxide were found to be too high. A carbon-dioxide content of 3% was thought to be tolerable, a notion based on short-term experiments. Prolonged exposure to a content of 3% carbon dioxide was found to produce deleterious effects on performance and physiologic functions. Systematic investigations of the effects of carbon dioxide were started for the purpose of establishing adequate limits of tolerance of carbon dioxide for extended periods of exposure. It was found that the respiratory pattern is decisive for the respiratory response and the tolerance to carbon dioxide. It was also demonstrated that flicker-fusion frequency decreased and alpha blocking increased as the concentration of carbon dioxide increased. Measurements provide useful criteria for evaluation of the depressive efforts of carbon dioxide on the central nervous system.

Operation Hideout: "Operation Hideout" was a controlled experiment in which 23 men were confined in a submarine submerged at dockside for 58 days. Experience gained in previous studies on the effects of carbon dioxide were utilized in the planning of Operation Hideout, in which new data on limits of tolerance to prolonged exposure to low concentrations of carbon dioxide were obtained. Results of these studies served as a basis for the design of carbon-dioxide scrubbers in nuclear-powered submarines which maintain carbon dioxide in the atmosphere at acceptable levels.

Operation Hideout solved many problems, but also produced additional ones. Consequently, attempts were made to explore the mechanisms involved in adaptation to carbon dioxide. With the use of implanted electrodes in the brains of monkeys, the effects of various concentrations of carbon dioxide in unanesthetized animals were studied. It was found that carbon dioxide exerts a depressing effect on the electrical activity of the cortical areas and a stimulating effect on the hypothalamic areas. Dissociation of the effects of carbon dioxide were correlated with different metabolic reactions of different tissues. For example, exposure to carbon dioxide affected the electrolyte exchange and carbonic anhydrase activity of different tissues in a different way.

Current work includes studies of physiologic mechanisms in the presence of carbon-dioxide toxicity, Phase 1 of which concerns the effects of carbon dioxide on acid-base balance and electrolyte exchange.

Tissue carbon-dioxide dissociation curves of various organs of guinea pigs and rats have been established with the use of exposure to concentrations of carbon dioxide of 15%, 30%, and 50%. Investigations are carried out to determine whether observed differences in tissue carbon-dioxide dissociation curves are related to the previously observed individual organ differences in electrolyte exchange and blood content. Information obtained from these studies should provide a basis for the establishment of a carbon-dioxide dissociation curve of the whole animal. This is a requirement for a better formulation of time-concentration charts of the toxicity of carbon dioxide.

On-and-off effects of exposure to carbon dioxide have been compared in respect to excitability of the brain, transport of carbon dioxide, and electrolyte exchange. A relationship between seizures caused by withdrawal of carbon dioxide, and changes in carbon-dioxide tensions, rapid changes

in electrolytes and water in blood and tissues, appear to exist.

Phase 2 of these studies of physiologic mechanisms concerns lung-volume factors as related to the measurement of respiratory sensitivity to carbon dioxide.

Dr. R. C. Stroud carried out a project consisting of multiple correlation of data concerning 12 volunteers which revealed a fairly high degree of correlation ($r=0.85$) between residual volume and vital capacity, on the one hand, and the slope of the carbon-dioxide sensitivity curve, on the other. The possible significance of these relationships is suggested by the observation that, by the use of correlation methods, it is possible to predict resting ventilation and alveolar carbon-dioxide tension on the basis of the above lung volumes ($r=0.87$). Thus, it would appear that interpretation of the classic carbon-dioxide sensitivity curve must take into account a degree of control by pulmonary mechanical and mixing factors.

Phase 3 of these studies concerns endocrine response to carbon dioxide.

This study of the effect of exogenous epinephrine hydrochloride on the carbohydrate metabolism of the rat narcotized with carbon dioxide has been extended further to elucidate endocrine interrelationships. Hypophysectomized rats also were used in a similar study. Observations have been made which show that the return to a normal atmosphere from one containing 30% and 15% carbon dioxide causes drastic and extremely fast endocrine and metabolic changes. The effect of hypophysectomy and adrenalectomy on convulsions developing after transition from an atmosphere containing carbon dioxide to air is being studied. Normal rats were exposed to 15% carbon dioxide in 21% oxygen for periods of up to 15 days, followed by a recovery period of 15 days. The glycogen studies showed that the changes in stores of glycogen in the liver parallel those observed when the animals were exposed to 30% carbon dioxide in oxygen, but the cycles are spread out over longer periods. Again, as in the study done with 30% carbon dioxide in oxygen, the changes on recovery are drastic as compared with those during exposure.

Parathyroidectomized rats were exposed to 15% carbon dioxide for 15 days to elucidate the relationship of calcium and phosphorus to calcification. This material is being processed at present, and histologic examination of teeth and long bones is planned.

Physiology of Diving: It has been demonstrated that during descent a reversed carbon-dioxide gradient develops from the lungs to the blood. Adaptation to skin diving can be developed. It involves an increase in lung volumes, as demonstrated in instructors during their tour of duty at the Escape Training Tank, and an increase in the tolerance to carbon dioxide and low concentrations of oxygen.

Studies in Air Embolism: Results of animal studies produced the exact transpulmonary pressure gradients (intratracheal pressure minus intrapleural pressure) at which air embolism occurs, and showed that circulatory changes are not directly responsible for the development of air embolism.

Considerable evidence based on experimental findings, necropsy data and results of roentgenologic studies has been accumulated which indicates that localized intrapulmonary air trapping plays an important role in casualties during submarine-escape training. Additional experimental studies are being carried out presently to elucidate the mechanisms involved.

Comment

Much of last summer's effort was devoted toward preparation and planning for the First International Symposium on Submarine and Space Medicine, held here in September, 1958. The symposium was organized and designed to bring together authorities in the fields of submarine and space medicine for the purpose of integrating existing knowledge in these two

closely related fields of research. Existing problems were classified, and means for coordinating future efforts in fields of particular interest to the Armed Forces were established. The true submersible and the sealed-space cabin have in common a condition of prolonged confinement which presents formidable problems of environmental medicine. One of the fundamental problems facing workers in both fields is the lack of knowledge concerning the extent to which man is dependent upon the natural composition of the earth's atmosphere.

Topics of discussion in this symposium had to be limited. Selected were those environmental changes which are known to play a role under conditions of prolonged confinement (low and high carbon dioxide, variations in pressure, nitrogen, ozone, gravity-free state, sensory deprivation, trace substances). Effects of heat and cold, as well as of radiation and acceleration, had been dealt with in numerous recent symposia and thus were omitted.

To achieve integration of knowledge, the effects of various changes in the atmosphere upon the main physiologic systems (circulation, respiration, and the central nervous system) were discussed in individual sessions on consecutive days, leading to a presentation of the more general problems of human ecology on the final day. The proceedings, being published by American Institute for Biological Sciences, are now in press and will be available soon.

Future studies will concern human ecology in confined spaces simulating conditions of the true submersible. With the advent of the true submersible and the sealed-space cabin, hitherto unknown, man-machine systems have come into existence. The reliability of the functioning of these systems depends to a large extent on the limitations offered by the human component. The design engineer has to take the medical-physiologic aspects into account for his planning to assure compatibility of the programed functions of the whole system with the limitations of the human factor. In a closed ecologic system, such as in a submarine under conditions of prolonged submergence for several months, three important limitations of human functions exist: (1) physiologic and psychologic manifestations of the day-and-night cycle; (2) sensory deprivation, and (3) reduced expenditure of energy. In addition to these limitations of human functions, there is also the limitation effected by the changes in the atmospheric components of carbon dioxide, carbon monoxide, and ionization and trace substances, including ozone.

Research into human ecology in confined spaces should be oriented to provide an adequate knowledge of these four limitations of human functions. It is planned to carry out the following studies in a newly developed climatized pressure-altitude chamber.

Study of Diurnal Cycles of Physiologic Functions Under Conditions of Confinement and Atmospheric Changes.—It is expected that changes in diurnal cycles could be utilized as early indices of general fatigue and approaching breakdown under conditions of confinement.

Cybernetics of Simulated Cycles in Closed Spaces.—Recently, research activities in the field of diurnal cycles have increased considerably because of the recognized importance of such research in medicine, especially in the performance of work in industry. Reports of extensive investigations of diurnal cycles in shift workers were given at the International Congress of the Society for the Study of Biological Cycles in Stockholm in 1955. The programing of work and the planning of shifts in industry have begun to take into account the limitations set by the diurnal cycles which cannot be broken or eliminated. Under conditions in which the cyclic elements of nature are reduced, external timegivers like light and darkness and temperature are utilized to simulate the external 24-hour cycles.

Study of Sensory Deprivation and Its Alleviation.—Reduction in the normal sen-

sory stimulation components of the environment is a potential problem in submarines operating for long periods. It is partly connected with the missing natural cyclic components in the submarine environment. The investigation will seek to determine whether the introduction of external timegivers is sufficient to stimulate the diurnal cycles of physiologic functions and to maintain a normal or adequate sensory input, or whether some special kind of sensory stimulation would be necessary.

Study of the Effect of Reduced Expenditure of Energy on Physiologic Functions and Performance.—Studies carried out in "Operation Hideout" during which 23 volunteers were confined for 58 days in a sealed submarine and exposed to a low concentration of carbon dioxide for 42 days indicated that the reduced expenditure of energy represents an important problem under conditions of confinement, and a problem which warrants additional investigation. Man is built for a certain amount of movement and expenditure of energy which provide a stimulus for metabolism, production of heat, circulation, and respiration.

The results of these studies will be important in their application to extended submarine operations, to the "man-in-space" program, and to the construction of civil defense shelters.

Thus, in the second decade of its life, the Naval Medical Research Laboratory, as shown by this review, endeavors to make the fulfillment of its mission an "all-hands" effort to augment the effectiveness of the Submarine Force. The preceding pages, which outline our planned instructional, training, and research work, leave untold some other time-consuming and important activities. We circulate a considerable volume of scientific literature, and receive requests for reprints of papers from all over the world. We receive large numbers of visits from Naval officers and other military personnel of the United States and NATO. Frequently, civilian and military scientific committees or consultant groups hold their meetings in our quarters. And we are visited by representatives of numerous industrial agencies seeking special information relevant to their government contract work. Members of our staff are frequent speakers before scientific societies and miscellaneous civilian groups. Our task is always a developing one; it is never done.

The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or reflecting the view of the Navy Department or the Naval Service at large.

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Effect of Perphenazine on Postoperative Emesis

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Emesis during the immediate postoperative period creates three major hazards: dehydration, electrolyte imbalance, and delayed alimentation. In addition the stress during retching and vomiting may disrupt fresh wounds, in particular those of the upper abdomen. It therefore seems desirable to seek medication which may offer alleviation of this rather common aftermath of systemic anesthesia and surgical therapy.

Attempts to protect dogs against vomiting induced by apomorphine have shown that perphenazine has significantly greater antiemetic potency than other phenothiazines in current use.[1,2] In the human, clinical experience reported by others[3-5] supports its effectiveness. Prophylactic or therapeutic administration of perphenazine has been shown to be extremely effective when given parenterally before or after surgery to protect against postoperative emesis. In double-blind studies among surgical patients, perphenazine reduced the incidence of emesis from 18% to 6% in a series of 610 patients,[6] from 48% to 25% in a series of 201 patients,[7] and from 21% to 7% in a series of 200 patients.[8] In each of these studies, half of the patients had received perphenazine, and half a placebo, intramuscularly. Dosage was, respectively, 11.25 mg. in three divided doses,[6] 10 mg. in two divided doses,[7] and single doses of 5 mg.[8] These investigators commented upon the absence of arterial hypotension and other significant side-effects.

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Methods *

A consecutive series of 108 patients, 57 males and 51 females ranging in age from 14 to 74 years, was studied (Table 1). These patients were representative of an average surgical population (Table 2). Various combinations of thiopental, cyclopropane, and nitrous oxide were used for anesthesia (Table 3). The mean average duration of surgery was one and one-half hours. Four groups were established: 14 patients (Group 1) did not receive perphenazine; 32 patients (Group 2) received perphenazine therapeutically only if vomiting had occurred; 32 patients (Group 3) received perphenazine preoperatively, and 30 patients (Group 4) received perphenazine one hour postoperatively. A single dose of 5 mg. was administered intramuscularly in Groups 2, 3, and 4. Administration of perphenazine was deliberately limited to a single dose of 5 mg. despite the fact that repeat doses seemed indicated in a few patients. For some analyses Groups 1 and 2 were combined to determine the free incidence of vomiting and Groups 3 and 4 were combined to form the total treated group.

* Perphenazine (Trilafon) was provided for this study by the Schering Corporation, Bloomfield, N. J.

TABLE 1.—*Emesis in 108 Surgical Patients*

Administration of Perphenazine	No. of Patients M	No. of Patients F	Age Range, Yr.	Mean Age, Yr.	Mean Duration of Surgery, Hr.	Nausea or Vomiting
Group 1 (untreated)	10	4	29-56	43.9	1 ½	9 (64%)
Group 2 (treated only if needed)	13	19	14-72	45.3	1 ¼	16 (50%)
Summary, Groups 1 & 2 (controls)	23	23	14-72	44.6	1 ⅜	25 (54%)
Group 3 (treated preoperatively)	21	11	19-74	47.5	1 ½	4 (12%)
Group 4 (treated postoperatively)	13	17	14-72	40.2	1 ¾	3 (10%)
Summary, Groups 3 & 4 (treated)	34	28	14-74	43.9	1 ⅝	7 (11%)

TABLE 2.—*Summary of Surgical Procedures*

Type of Surgery	Group 1	Group 2	Group 3	Group 4	Total
Hemorrhoidectomy	0	6	7	4	17
Herniorrhaphy	4	3	5	5	17
Cholecystectomy	0	4	3	4	11
Minor procedures, rectal	3	5	2	1	11
Appendectomy	2	2	1	3	8
Minor procedures, extremities	1	2	2	1	6
Thyroidectomy	2	2	2	0	6
Gastrectomy	1	1	2	1	5
Repair of fractures or dislocations	0	3	0	2	5
Colostomy	1	1	1	1	4
Mastectomy	0	1	1	2	4
Excision of breast tumors	0	0	1	2	3
Repair of veins	0	1	1	1	3
Repair of tendons	0	0	2	0	2
Closure of cecostomy	0	0	1	0	1
Dilation and curettage	0	1	0	0	1
Excision of lymph nodes	0	0	0	1	1
Excision of melanoma	0	0	0	1	1
Resection of colon	0	0	1	0	1
Splenectomy	0	0	0	1	1
Summary	14	32	32	30	108

Results

The incidence of nausea or vomiting did not differ significantly between Group 1 and Group 2 (64% and 50% respectively). Results in the group of patients who received perphenazine preoperatively (Group 3) did not differ significantly from those obtained in the group who received the drug postoperatively (Group 4). The incidence of nausea and vomiting was 12% and 10% respectively. Postoperative administration tended to make some patients drowsy during the first hours after surgery, an effect which was rather marked in 6 of 30 patients in Group 4. The over-all incidence of nausea and vomiting was 54% (25 of 46 patients) in the consolidated control group and 11% (7 of 62 patients) in the consolidated treated group.

The effect of perphenazine used therapeutically was evaluated by comparing results in Group 1 with those in Group 2. Of the nine patients in Group 1 (untreated) who complained of nausea and/or vomited, the mean average duration of symptoms was 12.9 hours. No records were kept of when Group 2 patients reported symptoms and received the drug. Of the 16 patients in Group 2 with nausea and/or vomiting, symptoms ceased within a mean average of 36 minutes, and in 13 patients (81%)

TABLE 3.—*Correlation of Anesthesia with Emesis*

Type of Anesthesia	Group 1		Group 2		Group 3		Group 4	
	No. of Patients	No. Vomiting	No. of Patients	No. Vomiting	No. of Patients	No. Vomiting	No. of Patients	No. Vomiting
Thiopental, cyclopropane, nitrous oxide, oxygen, ether	0	—	0	—	0	—	1	0
Thiopental, cyclopropane, nitrous oxide, oxygen	0	—	1	1	0	—	0	—
Thiopental, cyclopropane, oxygen, ether	3	2	3	2	3	0	2	0
Thiopental, cyclopropane, oxygen	3	3	3	2	4	1	8	0
Thiopental, cyclopropane	0	—	0	—	0	—	1	0
Thiopental, nitrous oxide, oxygen, ether	0	—	1	0	3	0	3	1
Thiopental, nitrous oxide, oxygen, spinal	0	—	0	—	0	—	1	0
Thiopental, nitrous oxide, oxygen	1	0	7	3	2	0	2	0
Thiopental, nitrous oxide	0	—	0	—	0	—	1	0
Thiopental, oxygen, ether	0	—	1	1	3	2	1	0
Thiopental, oxygen	0	—	0	—	0	—	1	0
Thiopental, caudal	1	0	2	1	3	0	2	1
Thiopental, general	0	—	0	—	1	0	0	—
Thiopental, spinal	1	0	2	1	1	0	0	—
Cyclopropane, nitrous oxide, spinal	0	—	0	—	1	0	0	—
Cyclopropane, oxygen, ether	0	—	1	1	2	0	2	0
Cyclopropane, oxygen	0	—	2	1	0	—	0	—
Caudal	0	—	4	1	2	0	0	—
General	4	3	3	1	2	0	2	1
Spinal	1	1	2	1	5	1	2	0
Spinal, oxygen, ether	0	—	0	—	0	—	1	0
Summary	14	9	32	16	32	4	30	3

within 30 minutes, after administration of perphenazine. In the seven affected patients in Groups 3 and 4, the mean average duration of symptoms was 7.5 hours, and the character of the disturbance was clinically less severe.

The patients in Group 1 were able to take fluids by mouth after a mean average of 13.8 hours, whereas the patients in Groups 3 and 4 tolerated fluids after a mean average of 7.1 hours.

Comment

These results, which parallel those obtained by previous investigators,[6-8] indicate that prophylactic administration of perphenazine reduced the incidence of postoperative emesis to less than one-fourth of that which occurred in untreated patients. The treated patients tolerated oral fluids more rapidly than did those included in the controls.

In those few patients in whom emesis was not prevented entirely, perphenazine apparently reduced the severity and duration of symptoms. It is possible that complete protection would have resulted from additional or higher doses of the drug in these patients.

Perphenazine acts rapidly to relieve emesis, whereas in patients who are not treated the symptoms persist for a longer period of time. In one obese woman with an incisional herniorrhaphy (Group 2), it was especially important to avoid stress against the sutured wound. This patient was retching in the recovery room until perphenazine was given. Relief occurred in 10 minutes, followed by sleep for 6 hours. The patient was able to take fluids by mouth upon awakening.

Postoperative arterial hypotension occurred in one patient. It is believed that this was due to postoperative hypovolemia, which was easily corrected by use of Trendelenburg's position and intravenous administration of fluids.

A number of desirable effects attributable to perphenazine were noted in the treated groups. Patients were relaxed and comfortable although vital signs were not depressed. There was some reduction of motor activity, but this was not excessive. Hyperactivity was not exhibited by any patient.

Although both pre- and postoperative administration seem to be of approximately equal effectiveness in the prophylaxis of postoperative emesis, there appear to be certain advantages to preoperative administration of the drug. It has been shown that the requirements of meperidine and anesthetics seem somewhat less, and induction of anesthesia is smoother.[9] Both of these considerations are especially important in poor-risk patients.

Summary and Conclusions

Prophylactic intramuscular administration of perphenazine significantly reduced the incidence of postoperative nausea and vomiting in the series of patients reported. Either preoperative or postoperative administration is effective in reducing the incidence of emesis after surgery. Emesis occurred in 54% of a control series of 46 patients but in only 11% of the treated series of 62 patients. When emesis did occur among treated patients, the total period of nausea and vomiting was shorter in duration, and the individual attacks were less severe and less frequent.

Patients who received perphenazine tolerated fluids by mouth earlier than did those in the control series.

Perphenazine also proved to be effective in the treatment of postoperative patients with nausea or vomiting. Emesis usually ceased within 30 minutes after administration of the drug.

There appeared to be no hypotensive effect attributable to perphenazine. Patients who received perphenazine were generally more relaxed and comfortable during recovery. In addition, postoperative administration seems to cause drowsiness, an effect which is usually desirable.

60 Remsen St.

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The Relationship of Fibrocystic Disease to Carcinoma of the Breast

A Study Based on Eight Hundred Seventy-Six Cases

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Since the publication of lectures by Sir Astley Cooper,[9] Brodie,[4] and the classic observations made by Reclus,[25] numerous reports have appeared in the literature on the relationship of fibrocystic disease to carcinoma of the breast. The condition is referred to by various names—chronic cystic mastitis,[20] Schimmelbusch's disease,[28] adenocystic disease,[1] lobular hyperplasia,[29] simple cystic disease of the breast, and other designations.[3,15,23,31] Convincing proof that this disease is pathologically related to carcinoma has not been established. The uncertainty and varied ambiguous premises advanced relative to the malignant transformation of fibrocystic lesions of the breast have served as a stimulus for this report.

Fibrocystic disease of the mammary glands is the commonest of all breast lesions and primarily affects females but may occur in males.[18,30] It is characterized clinically by pain or a lump in the breast and pathologically as a fibroglandular hyperplasia, localized or generalized, cystic or noncystic.

The observations and conclusions recorded in this paper are based on a study of 876 unselected cases of breast lesions. Of these 466 were clinically and pathologically initially diagnosed as fibrocystic disease and 410 conclusively established as carcinoma. Two approaches were employed in attempting to establish the incidence of benign fibrocystic mammary lesions undergoing malignant transformation—(1) the review of cases which were initially diagnosed as benign and which subsequently developed carcinoma, and (2) the review of cases pathologically established as carcinoma which developed typical cystic or fibroglandular hyperplasia either prior to malignant change or concomitantly associated with it at the time of operation. The incidence of malignant transformation in the total series of 876 cases was 3.1%. Of the total group of 466 benign fibrocystic lesions (Group I), 2.1% subsequently developed carcinoma, whereas, in the series of 410 malignant lesions, 27 (Group II), or 6.6%, were found to have had coexisting or preexisting fibrocystic changes.

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Anaylsis of the Cases

The data were obtained from records of 876 carefully worked up, unselected cases followed by the Tumor Clinic of a teaching hospital for a period varying from 1 to 28 years. Follow-up information was usually secured directly from examination of patients every four to six months. When patients could not attend the tumor clinic, the follow-up information was secured indirectly by correspondence with the patient and her physician.

Whenever surgical intervention was employed, frozen section of the surgical excisional biopsy specimen was obtained and complete pathological report was incorporated into the patient's record.

Presentation of the Data

The follow-up period for the benign group ranged from 1 to 28 years; 361

(77.4%) of the patients in Group I were followed for more than 7 years, and the average period was 9.1 years. For the 410 originally malignant cases, the follow-up ranged from 2 weeks to 17 years, the average being 4.5 years.

Incidence

Age.—In the 466 cases of fibrocystic disease (Group I) the age incidence ranged from 13 years to 80 years, with an average of 39.5 years for the entire group. The average age of the 27 patients with carcinoma (Group II) was approximately 51 years. The age incidence varied from 19 to 81 years.

Sex.—In the benign group there were 434 females and 32 males. All of the patients who had malignant lesions associated with fibrocystic changes were females.

Race.—In the benign group (Group I) 74% were whites and 26% were Negroes. Of the malignant group (Group II) 24 patients were of the white race and 3 of the Negro race.

Distribution and Site of Involvement (Table 1)

In Group I the distribution of the fibrocystic process was unilateral in 62.5% of cases, and the left breast was implicated more often than the right. The upper outer quadrant was the site of involvement in 60% of the patients.

Similarly in Group II, the incidence was predominantly unilateral, involving the upper outer quadrants of the breast. In contrast to the benign group, the right breast was more frequently the location for malignancy, being involved in approximately 63% of the cases.

TABLE 1.—*Distribution of Disease*

Group No.	Right Breast	Left Breast	Bilateral	Total % Unilateral	Total % Bilateral
I. Benign (466 cases)	124	168	174	62.66	37.34
II. Malignant (27 cases)	16	10	1	96.3	3.7

In both groups, the unilateral distribution was localized, whereas bilateral involvement was commonly diffuse.

Clinical Features

Group I.—The most frequent first symptom and chief complaint of the patient was a lump in the breast. This was the first complaint in approximately 73% of the benign cases studied. The breast masses were often unilateral, irregular, coarse or shotty, and less frequently the tumor mass was discrete and firm or the breasts presented a generalized thickening.

Painful breasts associated with menses was the chief complaint in 51% of Group I. Usually the history revealed pain and tenderness of the breasts occurring premenstrually and terminating shortly after the onset of menses. In others, the mammary pain was unassociated with the menstrual cyclic changes, and this accounted for the initial complaint in 8.4% of patients with benign lesions.

A history of nipple discharge was elicited in 10.9%. The appearance varied from serous to serosanguineous, and a bloody discharge was noted in a third of the cases. Duct papilloma was the lesion in the benign group most commonly associated with this type of discharge. Of the total number of 19 duct papillomas associated with fibrocystic changes, 17 presented bloody discharge as a major complaint.

Nipple retraction, inversion, and dimpling of the overlying skin was infrequently noted. A history of trauma was elicited in 4.5% of Group I.

Group II.—In the malignant cases, the symptoms of onset in their order of frequency were noted as follows: a painless lump in the breast in 16 patients, pain associated with a lump in 6, painful breasts in 8, nipple discharge and bleeding in 2 cases, a history of trauma in 2, and 1 patient presented no symptomatology but a breast lesion was detected at a routine physical examination. A familial history of carcinoma was obtained in 6 of the total series of 27 cases.

TABLE 2.—*Types of Treatment*

Group No.	Total No. Operations	Total No. Patients	Types of Treatment: Excisional Biopsy	Partial Mastectomy	Simple Mastectomy	Radical Mastectomy	Incision & Drainage
I. Benign * (466 cases)	307	294	242	18	32	11	4
II. Malignant (410 cases)	59	27 †	28	3	4	24	—

*Total no. of patients treated by nonoperative means, 172.
† Total no. of patients presenting fibrocystic breast changes associated with carcinoma, 27.

The size of the mass varied from 1.5 to 12 cm., and it was frequently firm, irregular, localized, and nontender. In approximately 25% of the patients, carcinoma was fixed to either the overlying skin or underlying pectoral muscles and fascia.

Of the 27 patients in this group, 5 demonstrated dimpling of the overlying skin and in 3 there was retraction of the nipple, whereas in 4 axillary lymphadenopathy was found.

Accessory clinical studies, i. e., pulmonary and osseous roentgenographic surveys revealed no evidence of carcinoma or metastasis in the majority of cases. Pleural effusion in one, and peribronchial lung thickening in another was noted.

Forty-five per cent of the patients were anemic, and in three cases the alkaline phosphatase was elevated.

Treatment (Table 2)

Group I.—Various forms of therapy were utilized in the management of these patients. Operative intervention was employed in most of the cases, and 307 operations were performed upon 294 patients; 172 (37%) patients received either conservative or no treatment.

Excisional surgical biopsy with immediate frozen section analysis constituted 80% of the total number of surgical procedures. This was usually followed by radical mastectomy if the lesion was malignant. Bilateral procedures were done in 18 patients undergoing surgical excisional biopsy, in 2 of the patients with partial mastectomy, and in 5 of the simple mastectomy group.

Of the total 172 patients not operated upon, 46% received conservative therapy (i. e. heat, brassiere support, ointments, and so forth), 6.3% roentgenographic and 7.5% endocrine therapy. Of this group, 68 patients received no therapy, but follow-up examination every four months was maintained.

Group II (Table 2).—The total number of operations performed on 27 patients of the total series was 59.

Surgical excisional biopsy was performed in 100% of the patients with malignancy; 89% had radical mastectomy, and one patient had simple mastectomy performed because chest roentgenograms revealed metastasis.

Pathology

The terms utilized in the pathologic diagnosis of benign breast lesions of the fibrocystic variety have been classified by the Department of Pathology at Jefferson as fibroglandular hyperplasia, sclerosing adeno-

TABLE 3.—*Pathologic Classification of 307 Cases of Fibrocystic Disease of the Breast in Group I (466 Cases)*

Typical Cystic Hyperplasia	Per Cent Total	Fibroglandular Hyperplasia	Per Cent Total	Sclerosing Adenosis	Per Cent Total	Physiological Hyperplasia of Pregnancy	Per Cent Total
192	62.6	63	20.5	48	15.6	4	1.3

sis, typical cystic hyperplasia, and physiological hyperplasia. This classification has been in existence at this institution for the past seven to eight years.[11] Prior to that they were grouped together under the diagnosis of cystic mastitis or cystic hyperplasia. The term mammary duct ectasia introduced by Haagensen is not used here.

A pathological diagnosis was obtained in approximately 65% (307) of 466 cases in Group I. These are shown in Table 3.

There were 78 pathologically proved associated lesions, the commonest being fibroadenoma and the least frequent carcinoma.

The pathologic findings described below, although different somewhat in microscopic appearance, are all modalities of the disorder of the breast referred to by some as chronic cystic mastitis and cystic hyperplasia and more recently by others as mammary dysplasia. Clinically, and very likely also etiologically, they are therefore one entity.

1. *Typical Cystic Hyperplasia* (Fig. 1).—This is characterized grossly by various-sized cysts, some of which may be "blue-domed," and by more prominent increase in fibrous tissue. It represents a more advanced stage of mammary dysplasia. In many areas abundant pasty semisolid material can be expressed from dilated ducts. Microscopically, the epithelium lining the larger cysts is often flattened and atrophic and may even disappear altogether in areas. Papillary or non-papillary ductal hyperplasia is discernible in areas where the cysts are of smaller size. Apocrine-like epithelium may be present; the lining cells of these ducts are acidophilic, tall cuboidal, and possess well-delineated basilar pale-staining nuclei.

2. *Fibroglandular Hyperplasia.*—This has been called by others mazoplasia and mastodynia. The mammary tissue is finely granular; its consistency is increased, and its stroma is irregular and denser than normal. Microscopically, the lobules are ir-

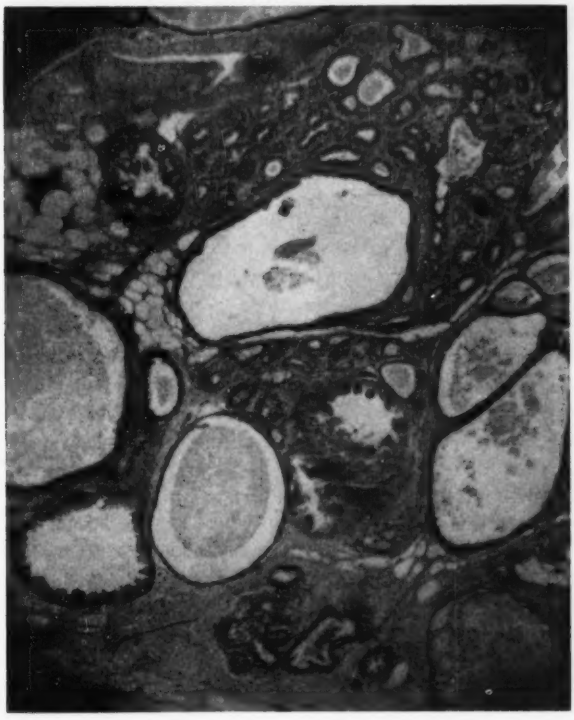

Fig. 1.—Typical cystic hyperplasia. The various-sized cysts are empty or filled with amorphous debris; their lining varies from a single, indistinct layer of flattened cells to a well-delineated, pink cuboidal epithelium thrown into small papillary infoldings. Hematoxylin and eosin; × 50.

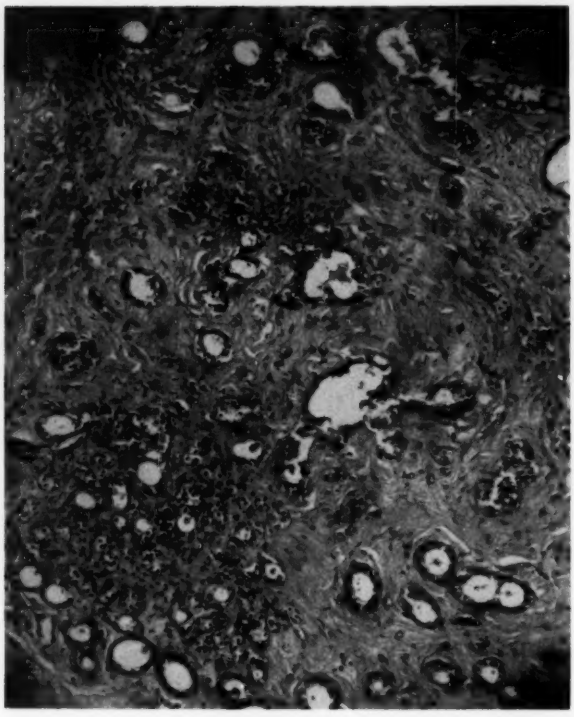

Fig. 2. — Sclerosing adenosis. Bundles of avascular, poorly cellular connective tissue permeate freely among mammary ducts. Some of the latter appear collapsed and compressed by the fibrous tissue, whereas others retain a distinct lumen. Hematoxylin and eosin; × 100.

regular, increased in size, the latter varying considerably in the same lesion. The ducts are microscopically dilated, but true cysts are absent. Deviation from normal is not marked, but the parenchyma is somewhat hyperplastic and the stroma more abundant and denser.

3. *Sclerosing Adenosis* (Fibrosing Adenosis, Adenosis, Fig. 2).—Grossly, the gland is prominently nodular and even firmer; cutting is done with difficulty. Microscopically, there is diffuse fibrosis, with permeation of the lobules by prominent bundles of fibrous tissue. Many ducts are moderately dilated and are either empty or contain varying amounts of clear fluid. The ductal epithelium is definitely hyperplastic and extends into the lumen as fine small papillary projections. The intralobular infiltration by fibrous tissue and the hyperplastic character of the ductal epithelium give an impression of invasiveness. This is the lesion of the breast more frequently confused with carcinoma; it is an uncommon type of mammary dysplasia.

4. *Physiological Hyperplasia* (Fig. 3).—Under this diagnosis are included the parenchymal and stromal changes of the female breast observed during pregnancy and lactation. The prominence of these changes varies with the trimester of pregnancy during which they are observed. In the most characteristic form (at term) they consist of lobular proliferation with acinar differentiation and distention of epithelial cells by prominent vacuoles of accumulated secretions. The stroma is loose and its vascularity is increased.

Twenty-nine tumors were present in 27 patients in Group II. Duct-cell carcinoma was the predominant type, occurring in 10 (37%) (Fig. 4), scirrhous carcinoma in 9 (33.3%) (Fig. 5), adenocarcinoma in 6 (22.2%), medullary carcinoma in 1 (3.7%), early comedo carcinoma in 1 (3.7%), infiltrating lobular carcinoma in

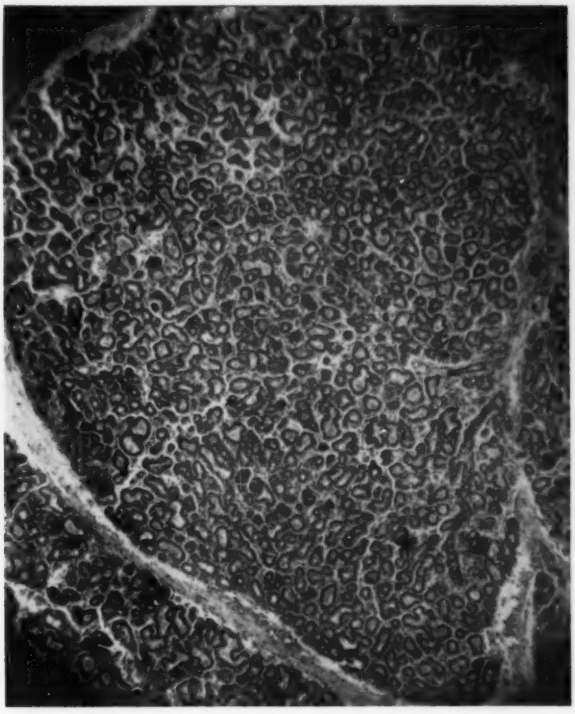

Fig. 3. — Physiological hyperplasia. Delineated by a thin septum of connective tissue, can be seen closely packed mammary ducts and alveoli. The presence of vacuoles in most of the lining cells denotes secretory activity. Hematoxylin and eosin; × 50.

1 (3.7%), and there was 1 case of Paget's disease of the nipple and breast. Scirrhous carcinoma was associated with duct-cell carcinoma in two cases. Five of the duct-cell carcinomas were of the intermediate type; six were metastatic to one or more axillary lymph nodes.

Comment

There are many reports in the literature concerning the important relationship of fibrocystic disease of the breast to mammary carcinoma. This relationship has been statistically studied on the basis of clinical follow-up observations by one group and pathological diagnosis and classification by the other group.

A number of authorities [3,7,9,14,26,28,32] believed that fibrocystic disease was a precursor to cancer. Cheatle,[7] on the basis of histological studies, described the process of cyst formation as desquamative epithelial hyperplasia which passed from benign to a malignant phase. He felt that this process accounted for 20% of all carcinomas of the breast. Cutler (1932)[10] concurred in this view. Bloodgood (1904 and 1906) on the basis of histological study, believed that malignant epithelial transformation occurred in 10% of all cases of cystic disease.

Rodman (1920)[27] advised radical mastectomy in older patients because of the frequent occurrence of cystic mastitis with carcinoma.

Warren (1940)[32] analyzed the data in two large groups of female patients who had been operated upon for fibrocystic disease. He found the subsequent incidence of breast carcinoma in these patients to be considerably higher than in women with no previous history of chronic cystic mastitis. He concludes from this that fibrocystic disease is precancerous.

A large number of authors oppose the view that fibrocystic disease is precancerous.[2,6,17,19,22,24,26]

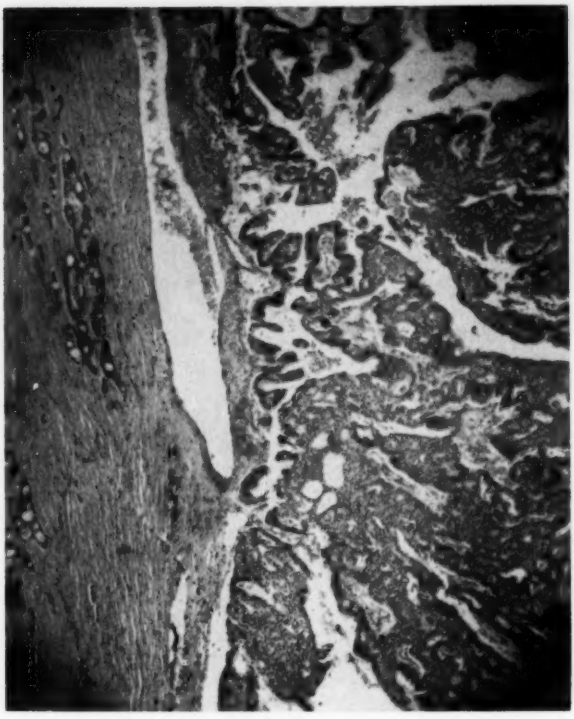

Fig. 4. — Infiltrating papillary ductal carcinoma. The bulk of the neoplasm projects in papillary fashion into the lumen of the duct, but there is unquestionable evidence of invasion through the base into the adjacent stroma. Hematoxylin and eosin; × 50.

Johnson (1925)[19] reported 107 cases of cystic lesions of the breast, of which 2 also had malignant lesions. In 47 patients who were subsequently followed, no cancer developed. Hart (1928) in a study of 104 benign and 24 malignant cases of intracystic papilloma regarded the former as benign if the base was not infiltrated and the cyst wall thin, with free mobility. Bloodgood in 1929 and Rodman in 1930 reversed their opinions, and on the basis of subsequent studies they concluded that this lesion was not precancerous and that the predisposition to the development of carcinoma in a previously involved cystic breast was no greater than in a normal one. Campbell (1934)[6] reviewed two series of cases totaling 290 cases of which 2 patients (0.7%) developed carcinoma. Lewis and Geschickter (1938)[22] studied two groups totaling 1,048 cases of chronic cystic mastitis. There were 523 cases that were followed for five years or more, and 4 of them, less than 1%, developed carcinoma. Palmer and Martin (1954)[24] reported a clinical study of 313 cases of proved carcinoma of the breast. Previous surgery for cystic disease had been performed in 2.23%.

Many factors have been implicated as possibly predisposing to the transformation of benign mammary fibrocystic lesions into carcinoma. They may be classified as congenital or familial, endocrine, mechanical or traumatic.

1. *Congenital or Familial Factor.*—There was a family history of carcinoma present in 22.2% of the patients in Group II, ranging from carcinoma of the colon to adenocarcinoma of the right breast.

2. *Endocrine Factors.*—There were several cases in Group I who had clinical and pathological evidence of fibrocystic disease of the breast which completely disappeared with pregnancy, lactation, and the onset of menopause. Several authors have made interesting experimental and clinical observa-

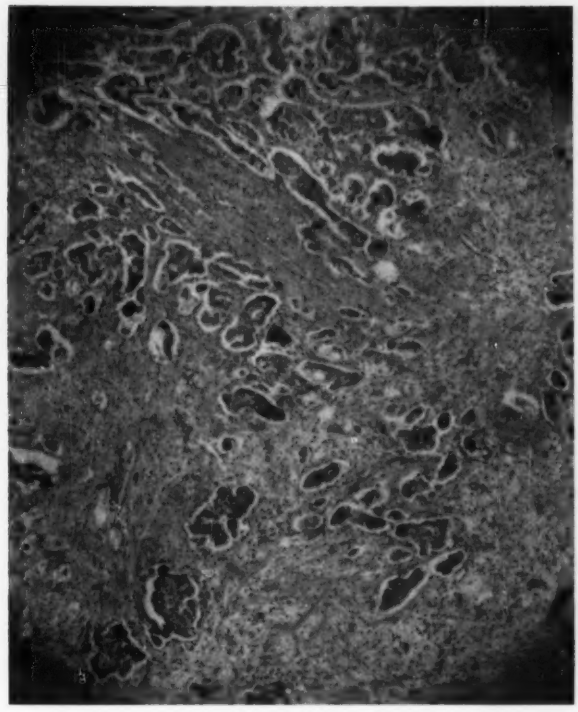

Fig. 5.—Scirrhous carcinoma. A carcinoma of ductal origin but at this stage freely invading the mammary stroma and productive of conspicuous fibrosis. Hematoxylin and eosin; × 50.

tions concerning the endocrine relationship of the ovary to cystic disease of the breast.[4-6,22,25]

3. *Mechanical Factors.*—Mechanical factors were associated with two of the cases of breast carcinoma associated with fibrocystic disease. One patient was a 29-year-old Negro woman who gave the history of having a blow sustained to her right breast from a swinging door. The other was a young secretary who had closed a file cabinet for several years with her chest. Both patients presented clinical and pathological evidence of carcinoma of the breast. After radical mastectomy this was confirmed histologically.

Summary

Eight hundred seventy-six cases of mammary lesions have been reviewed in an attempt to establish the relationship of fibrocystic disease of the breast to mammary carcinoma. The patients were divided into two groups: Group I, 466 cases diagnosed initially as fibrocystic disease, and Group II, 410 cases of previous mammary carcinoma.

In Group I, carcinoma was found associated with fibrocystic disease in 10 patients, 2.1%. This incidence is lower than that of the development of mammary cancer in the adult female population as a whole.[12,13] In Group II, 27 patients, 6.6%, had fibrocystic disease preceding or coexisting with carcinoma.

Factors possibly predisposing to the development of cancer from fibrocystic disease are discussed. In Group II 22% had a familial history of carcinoma.

The pathological type of fibrocystic disease most commonly encountered was the typical cystic hyperplasia variety, and fibroadenoma was the most frequent associated lesion. Duct-cell cancer and scirrhous carcinoma were the predominant pathologic types associated with fibrocystic disease.

The majority of cases in Group I and II were unilateral lesions, and the commonest site was the upper outer quadrant of the breast.

The majority of cases in Group I were treated by surgical intervention, surgical excisional biopsy being the commonest procedure utilized: 307 surgical operations were performed on 294 patients of the total group studied.

Conclusion

In the entire series of 876 patients the incidence of coexisting fibrocystic disease and carcinoma was 3.1%. This figure does not support the thesis that fibrocystic disease is precancerous.

Dr. Esther H. Montgomery, Research Associate, Department of Surgery, Jefferson Medical College, aided in the preparation of this manuscript.

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Pictorial Film Review

Techniques of Angiography

A. W. HUMPHRIES, M.D., Cleveland

This film has been produced in an effort to make visualization of the great vessels of the abdomen and of the extremities available to smaller communities. Standard x-ray facilities and a minimum of special equipment can produce diagnostic angiograms if utilized properly. Technique has been standardized so that comparable films may be produced under varying circumstances.

The demonstration of various forms of arterial disease, particularly the pattern of obstruction in occlusive arteriosclerosis, is of inestimable value in evaluating the type of treatment suitable for a particular patient. Safe, satisfactory intraluminal visualization of the major arteries is the best corroborative diagnostic tool available to substantiate a clinical diagnosis of arteriosclerosis obliterans.

In over 1,000 examinations, the only significant complication has been the unilateral loss of one kidney due to improper needle placement.

Cleveland Clinic.

Received for publication April 21, 1959.

Fig. 1.—An operating table is set up with a portable 14×17 in. 8:1 Bucky under the patient's abdomen and a Masonite-and-plywood 14×36 in. cassette holder under the lower extremities. A table such as the American Sterilizer No. 1080, which may be lowered close to the floor, is helpful.

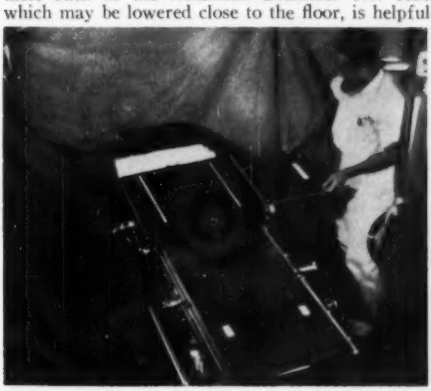


Fig. 2.—Although aortograms and femoral arteriograms may be done under local anesthesia, the pain of the injection frequently causes motion of the patient, with consequent blurring of the film. This may require a dangerous second injection. Therefore, general anesthesia is employed.

Fig. 3.—In aortography two 6 in. No. 18 needles are used with polyethylene extensions to permit the operator's hands to remain out of the direct field; 70% acetrizoate (Urokon) is the contrast medium presently utilized. Two needles, placed in parallel to the same depth, both of which are in an arterial blood-bearing vessel, prevent accidental injection of renal or mesenteric arteries.

Fig. 4.—A translumbar approach is made from the left side, just under the 12th rib, as for a left sympathetic nerve block. The needles are carried past the vertebrae about 1 in. and enter the aorta with a clearly recognizable puncture similar to that of entering the spinal canal in doing a spinal tap.

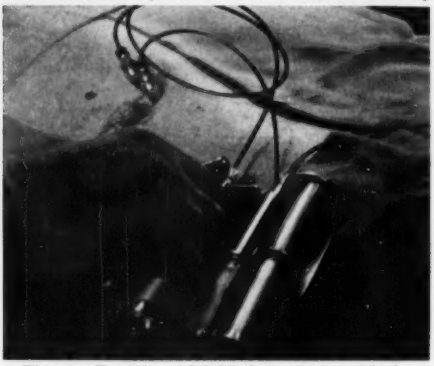


Fig. 6.—For ease of injection a homemade brass syringe holder permits emptying both 10 cc. syringes simultaneously. The 18 in. polyethylene extension tubing permits the operator's hands to be far enough from the central ray to make radiation hazard negligible.

Fig. 8.—A typical diagnostic aortogram is shown, clearly delineating an occlusion of the terminal aorta and a marked stenosis of the right common iliac artery. Note the clarity of visualization of the effective collaterals. Quality of artery—of surgical significance—can be easily evaluated.

Fig. 5.—When the needle stylet is removed, egress of freely moving bright red arterial blood indicates that the tip of the needle is in the aorta.

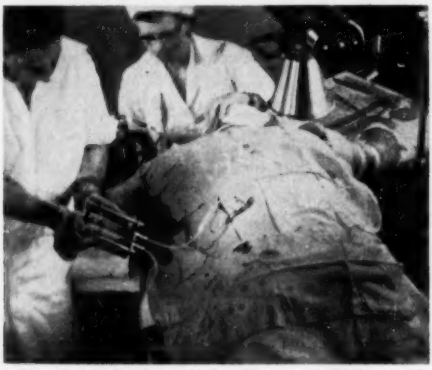


Fig. 7.—Injection of the 20 cc. of 70% acetrizoate is made as rapidly as possible, and the one-second x-ray exposure is timed to bridge the end of the injection. In the case of a known high aortic occlusion, the exposure may be delayed a second or two to permit more distal filling through collaterals.

Fig. 9.—The equipment needed for aortography is simple and usually readily available as standard equipment in most radiology departments.

EQUIPMENT	
OPTIMAL	200 MA PORTABLE WITH FULL RECTIFICATION, ROTATING ANODE TUBE, 2 MM. FOCAL SPOT
MINIMAL	50 MA PORTABLE WITH STATIONARY ANODE TUBE, 4 MM. FOCAL SPOT
PORTABLE 8:1 BUCKY 14" x 17"	
BUCK PARSPEED FILMS AND SCREENS	

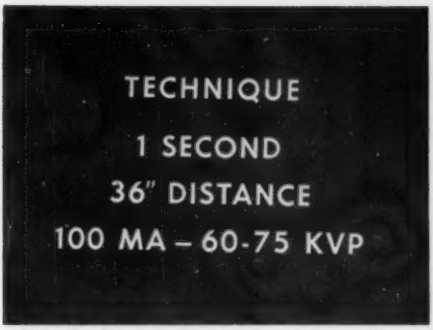


Fig. 10.—Exposure requirements are readily met with standard equipment.

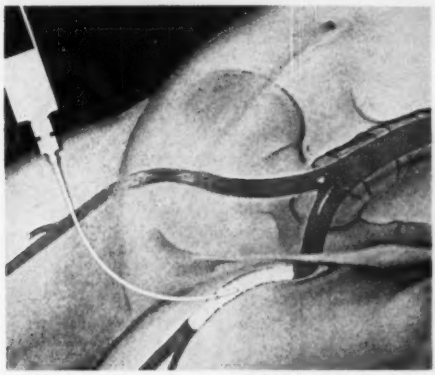


Fig. 12.—The retrograde injection of 20 cc. of 50% acetrizoate prevents accidental filling of only the superficial or the deep femoral artery, which can easily occur if the injection is done in a prograde manner. Also, isolated filling of the iliac system can be done if the femoral artery is manually occluded distal to the catheter at the time of injection.

Fig. 14.—A typical arteriogram, made on two 14×17 in. films placed end to end in a 14×36 in. cassette, is shown. Clear visualization from groin to lower calf is accomplished. The uniform density is attained by a wedge filter of 4 in. sq. aluminum, tapering from 0 mm. to 8 mm. in thickness, placed over the x-ray port.

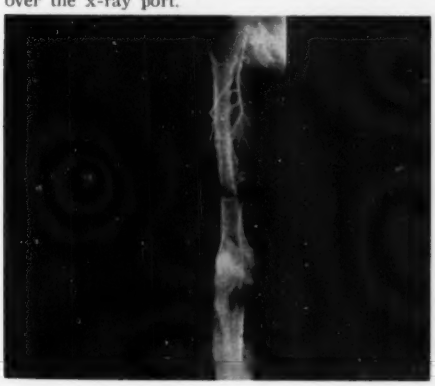
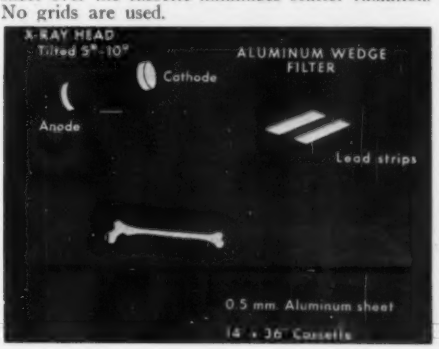
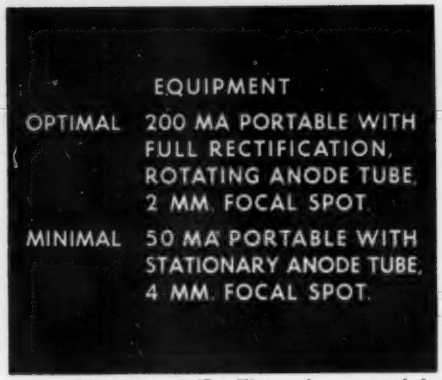


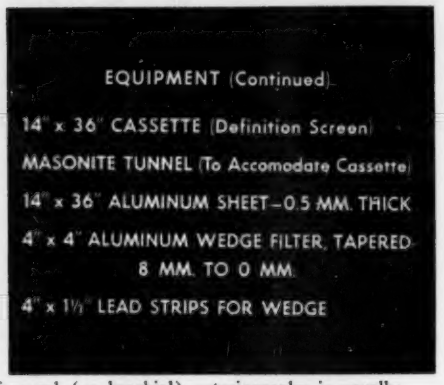
Fig. 11.—For femoral arteriography, or for retrograde aortography, a percutaneous catheter technique is employed. A heat-sterilized polyvinyl catheter is introduced retrograde into the common femoral artery through the bore of a thin-walled No. 14 needle, after which the needle is withdrawn over the catheter.

Fig. 13.—Injection again is accomplished with safety to the operator, since the 18 in. catheter permits the hands to be well out of the field. A slow injection of 10 to 12 seconds is used to permit the contrast medium to pass through collaterals well down into the lower leg. Exposure is made at the termination of injection.

Fig. 15.—This wedge filter, the lead strips on it to create the effect of a slit cone, and the placement of the x-ray head over the head of the femur with the anode cephalad and the head tilted distally 5 to 10 degrees permit the attainment of a full-length film of uniform density. The 0.5 mm. aluminum sheet over the cassette minimizes scatter radiation. No grids are used.




EQUIPMENT
OPTIMAL
200 MA PORTABLE WITH FULL RECTIFICATION, ROTATING ANODE TUBE, 2 MM. FOCAL SPOT.
MINIMAL
50 MA PORTABLE WITH STATIONARY ANODE TUBE, 4 MM. FOCAL SPOT.


EQUIPMENT (Continued)
14" x 36" CASSETTE (Definition Screen)
MASONITE TUNNEL (To Accomodate Cassette)
14" x 36" ALUMINUM SHEET–0.5 MM. THICK
4" x 4" ALUMINUM WEDGE FILTER, TAPERED 8 MM. TO 0 MM.
4" x 1½" LEAD STRIPS FOR WEDGE

Figs. 16 and 17.—The equipment used for femoral (or brachial) arteriography is usually available or readily manufactured locally. The thin-walled needle and matching catheter are commercially available.

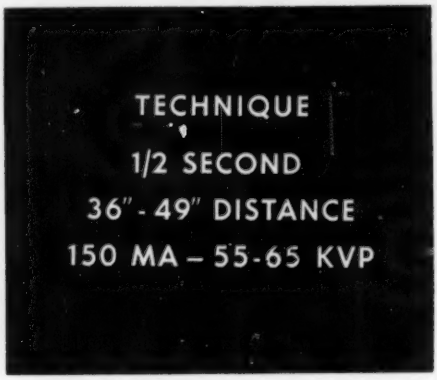


Fig. 18.—Exposure requirements are readily met with standard equipment.

Aortic Valvulography and Ascending Aortography*

WILLIAM MOLNAR, M.D.; SIDNEY W. NELSON, M.D.; KARL P. KLASSEN, M.D., and JOSEPH M. RYAN, M.D., Columbus, Ohio

Evidence in the literature and our experience indicate that the postoperative course after mitral valvulotomy is often unsatisfactory if complicating significant aortic insufficiency is present. It would therefore be useful to know how much deleterious influence early aortic insufficiency has on the results of mitral commissurotomy. In the presence of a diastolic murmur on the left side of the sternum there often is no reliable clinical evidence to differentiate between a Graham Steell type of murmur due to pulmonary hypertension and that caused by aortic insufficiency. A balanced electrocardiogram may even add to the difficulty. We therefore deemed it necessary to find a more exact way of differentiating between the two possibilities.

Accepted for publication April 13, 1959.

Departments of Radiology, Thoracic Surgery, and Cardiology of The Ohio State University Health Center.

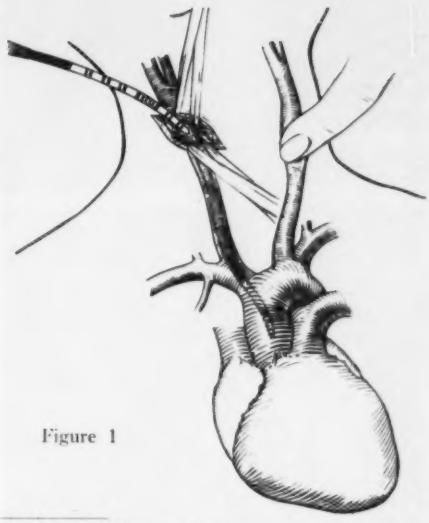


Figure 1

* Surgery Illustrated. Shown as a scientific exhibit of the Section on Radiology, at the 107th Annual Meeting of the American Medical Association, San Francisco, June 23-27, 1958.

Fig. 2.—Normal aortic valve remained competent at experimental studies in dogs if catheters with side opening were used for the injection.

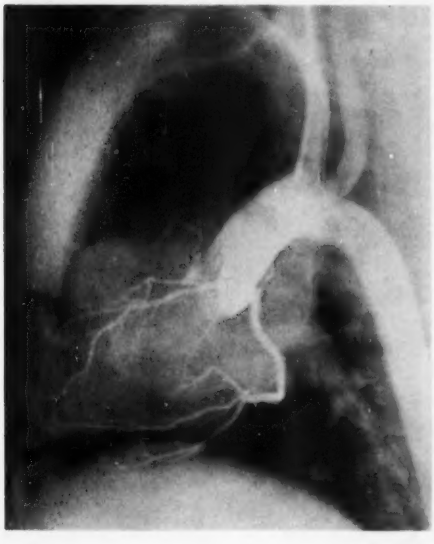
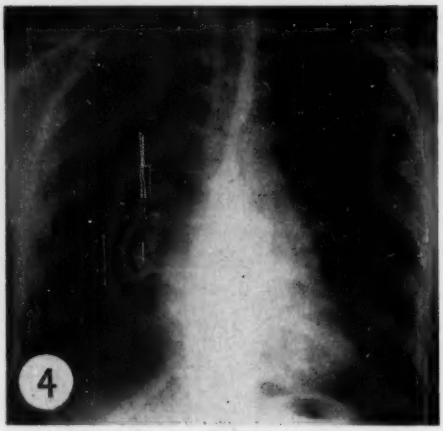
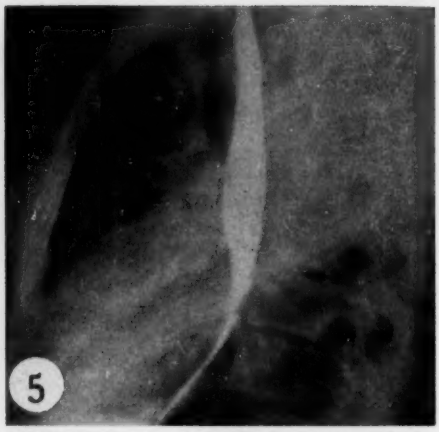
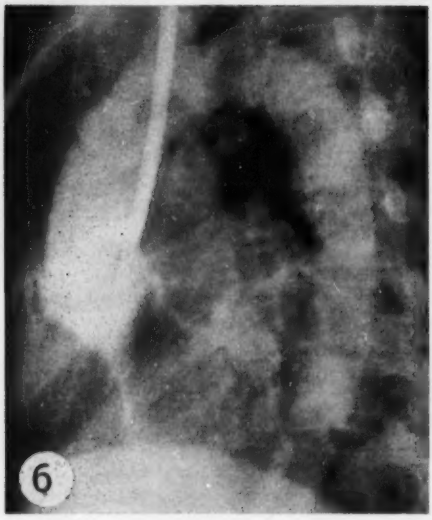
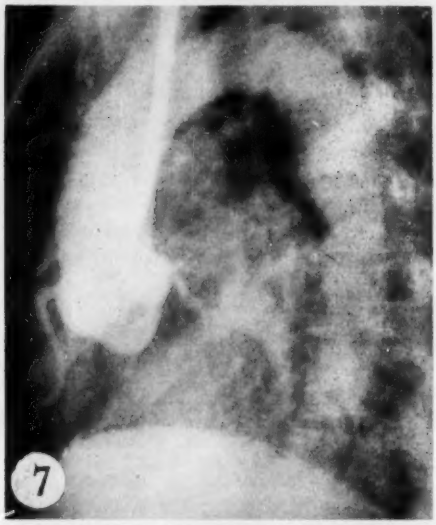


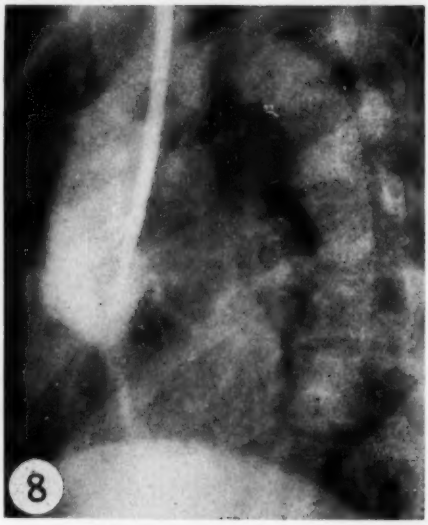
Fig. 3.—Follow-up films taken at 0.3-second intervals showed no regurgitation. Notice the good visualization of the coronary arteries.







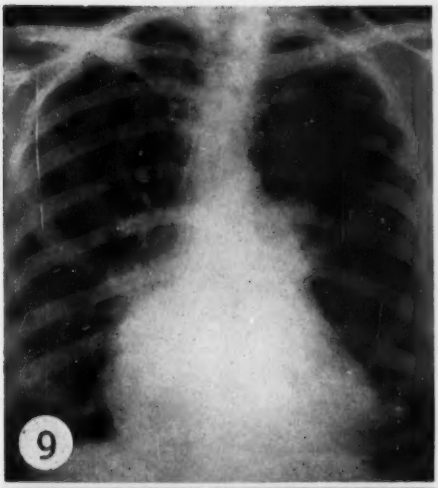


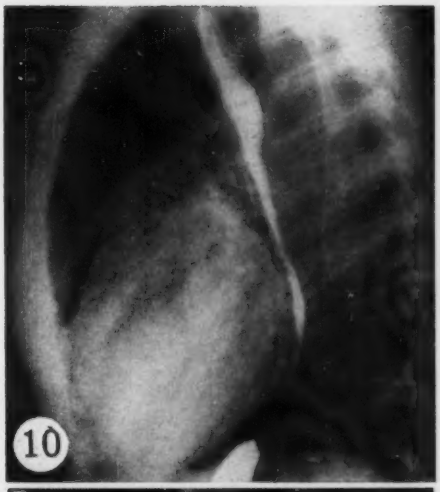


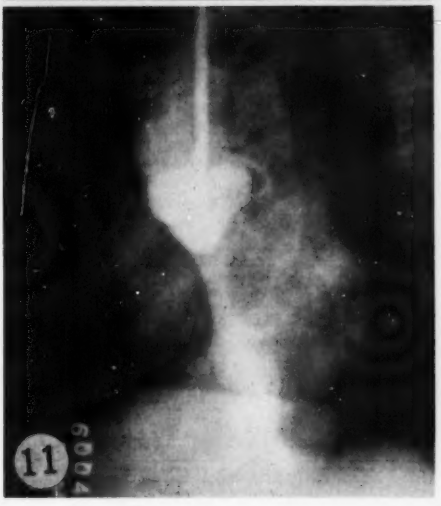
Figs. 4 and 5.—The clinical findings of mitral valve disease were complicated by the presence of a Graham Steell type of murmur. B. P 108/80. Chest films show characteristic features of mitral stenosis.

Figs. 6 and 8.—Serial films revealed mild regurgitation on every film taken during diastole.

Fig. 7.—Film taken during systolic phase showed no contrast below the valve.







Figs. 9 and 10.—Besides the murmurs of mitral stenosis and insufficiency, a loud diastolic murmur was heard over the pulmonic area in this case. B. P 120/90. Left ventricular and left atrial enlargement was suggested on radiographs.

Figs. 11, 12, and 13.—Continuous regurgitation of the contrast material in increasing amounts was visualized on serial films taken during injection.

Fig. 14.—Superior mediastinal mass was found on chest films of this patient, who had positive serology. Aortogram prior to contemplated surgery revealed aortic arch aneurysm also involving the innominate artery.

Fig. 15.—History of thoracic stab wound with subsequent clinical findings of intracardiac shunt. The site of the shunt could not be located at two previous thoracotomies. Aortogram showed direct communication between the right anterior cusp of the aorta and the infundibulum of the right ventricle.

Visualization of the aortic valve and demonstration of regurgitation into the left ventricle following injection of contrast material with use of conventional aortographic techniques usually gave unsatisfactory results because the material could not be injected rapidly enough to give good concentration. Aortography with the method demonstrated on the following pages gives constantly good visualization of the aortic valve and the regurgitation of the contrast medium in cases of aortic insufficiency. It also allows good visualization of the ascending aorta, very often not well seen by other methods. Note the demonstration of the coronary arteries.

To obtain base-line data for the technique of injection, at first a series of retrograde aortograms was performed on dogs; 21 studies were done on 13 dogs. Direct aortic pressures and electrocardiograms were obtained, before, during, and after the injection.

On the basis of this study a side-opening catheter was used in all of our human aortic valvulographies, with the tip of the catheter positioned approximately 1.5 cm. proximal to the aortic valve. The method and the results of these studies are described by us in detail in *The Journal of Thoracic Surgery* (32:46-52 [July] 1956) and in *Radiology* (70:697-712 [May] 1958).

Summary and Conclusion

A series of 51 retrograde aortograms was carried out on 49 patients in a period of three years. The cases examined belong to the following two major groups:

1. Sixteen injections were performed on 14 candidates for mitral commissurotomy (age group 21-54 years) to differentiate between aortic regurgitation and pulmonary insufficiency in the presence of a Graham Steell type of murmur. Of the 14 cases tested 9 had evidence of aortic insufficiency on the valvulograms. No accident or major complication to the test occurred in this group.

2. Thirty-five patients with different mediastinal and cardiac problems have been

given injections (age group 18-74 years) without fatality; however, one of the patients (72 years) developed a temporary left-sided hemiplegia lasting for six hours, and our oldest patient, a 74-year-old woman, became permanently paralyzed on the left side within two hours after the injection of contrast material.

We found the procedure very helpful in studying the function of the aortic valve, evaluating diseases of the thoracic aorta, and visualizing the coronary arteries.

Radiology Department, University Hospital.

The Use of a Barrier Cream to Protect the Skin from Irritating Discharges

ALAN RUBIN, M.D., Philadelphia

Patients who have leakage of urine or gastrointestinal contents, particularly material from the small bowel, often suffer considerably owing to excoriation of their skins. The number of patients with such distressing soilage is increasing, owing to the greater use of radical surgery and heavy irradiation, resulting in more ileostomies, "wet" colostomies, ureterostomies, and fistulas of the gastrointestinal and urinary tracts.

In an attempt to protect the skin from irritating discharges, we have employed the usual measures of early fitting with bags where possible, and the covering of the skin with zinc or aluminum pastes, egg albumin mixtures, kaolin, bentonite, or silicone preparations. Some of these local applications are messy and annoying to use. None has proved adequate in all cases, particularly where urine, or duodenal or ileal contents are involved. We therefore decided to try barrier creams of the variety which are employed in industry to protect the skin of workers exposed to various irritants. Counsell and Lockhart-Mummery[1] have mentioned the use of such a preparation in patients with ileostomies.

A barrier cream * which is effective against water-soluble irritants was tried in several patients whose skins had become badly excoriated despite much care. The patients reported relief of pain and burning after one or two applications. Visible evidence of improvement of the skin appeared within 24 to 48 hours.

The cream has now been used in 50 patients who have had skin soilage from one or more sources as indicated in the Table. The duration of use varied from four days to four months. The barrier cream was applied in a thick, even coating every three to four hours. An attempt was made to grade the effectiveness of the cream as excellent, good, fair, or poor.

The results were considered poor in only two patients. One of these had a duodenal fistula. The barrier cream gave inadequate

Submitted for publication March 16, 1959.

From the Gynecean Hospital Institute for Gynecologic Research and the Department of Obstetrics and Gynecology, School of Medicine and Hospital of the University of Pennsylvania.

* Kerodex 71 (Ayerst Laboratories), provided by Mr. Hugh Bennett and John B. Jewell, M.D.

The Effectiveness of a Barrier Cream in Protecting the Skin Against Irritating Discharges

Source of Drainage	No. of Patients *	Results			
		Poor	Fair	Good	Excellent
Ileostomy	15		1	4	10
Colostomy (transverse or right side)	23		1	6	16
Gastrostomy	1				1
Duodenal fistula	2	1			1
Ileal fistula	6		2	3	1
Ileal fistula (urine and feces)	4	1		2	1
Colostomy (urine and feces)	1				1
Total	52	2	4	15	31

* The number of patients is greater than 50 since some had more than one drainage site.

protection to the skin, while aluminum paste worked fairly well. The other patient had a perineal fistula draining urine and ileal contents. While the nursing personnel thought the cream was the best of the many preparations that had been tried in efforts to protect the skin, the patient preferred aluminum paste. Hence, the result here, too, was rated as poor. In four instances the protection was rated as fair. In all other cases the skin was well protected by the barrier cream, or improved in 24 to 48 hours if it had been in unsatisfactory condition previously. No patient had any subjective or objective evidence of irritation from the cream. In addition, it does not stain, and is esthetically highly acceptable. Since it is water-repellent, it is preferably applied to a dry surface. For best results it also should be permitted to air dry to a firm film for several minutes after application. This has proved to be its only disadvantage to date, for occasionally it is difficult to keep the patient's skin free of draining material long enough for the cream to dry. We have encountered no instances of local irritation or allergic reactions in the 50 patients studied despite the preparation's numerous ingredients (methyl- and propylparaben, sodium hexametaphosphate, isopropyl and cetyl alcohol, cetyl trimethyl ammonium bromide, partially sulfated cetyl-stearyl alcohol, petrolatums, paraffin, purified diatomaceous silica [Hydroflo Super-Cel], zinc oxide, kaolin, talc, precipitated calcium carbonate, D. & C. orange No. 4 and D. & C. red No. 10). It should also be of use in the management of incontinent patients.

Summary and Conclusion

A water-repellent barrier cream was evaluated in 50 patients with skin soilage from gastrointestinal contents or urine. Good protection of the skin was afforded in all but two instances. The cream is easy to apply, esthetically acceptable, and appears to offer better protection of the skin than any of the now commonly used preparations.

Medical Tower, 255 S. 17th St. (3).

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Sigmoidorectal Intussusception in Children

Recurrent Acute Attacks Without Incarceration or Obstruction

RICHARD H. TULLIS, M.D., and JOHN B. WELSH, M.D., La Jolla, Calif.

Our purpose is to list some clinical and anatomical states related to sigmoidorectal intussusception, and to report a case.

Acute attacks of sigmoidorectal intussusception cause lower abdominal, pelvic, or perineal pain, which starts suddenly and is relieved promptly by reduction of the intussusception.[7,12]

For at least 75 years proctologists have discussed sigmoidorectal intussusception, noting that procidentia occurs intermittently and rarely becomes incarcerated.[1]

Unstable colon, discussed by Granet, consists of a redundant sigmoid with a long mesentery. The sigmoid slides into a capacious rectum held in situ by fascia. Granet terms this a procidentia of the sigmoid and recommends conservative treatment.[2,3]

Chronic intussusception is a term used by some, decried by others.[4,5,13] Still's four cases (three ileocecal, one ileocolic) described in 1921 had intussusception verified to have existed from 21 to 42 days. Emaciation ensued, although other symptoms were mild after the onset. Each had surgical reduction with good results from one to eight years later.[14]

According to Kiesewetter and co-authors [4] chronic sigmoid intussusception was seen as the bleeding point in 18 of 143 cases of hematochezia in children.

Murdoch [8] mentions the terminal bowel syndrome, in which sigmoidorectal procidentia produces acute pain with each stool, prior to dilation of the sphincter ani. When the rectum is empty a sigmoidoscope can easily be inserted. Incarceration occurred in only two cases, both adults. In children the sigmoid readily descends at stool passage, spontaneously ascending shortly afterward.[9]

Megarectum as a sign of an obstructive lesion of the sigmoid has recently been cited by Witkowski and co-authors.[18] It has also been suggested that repeated enemata, incompletely expelled because of partial sigmoid obstruction, may produce megarectum.

On the basis of human dissections Todd [16] (1920) felt that the comparatively straight sacrum and vertical rectum of infants predisposed to the development of rectal prolapse. Within a few years both sacrum and rectum assume a more oblique angle with the perineum, correcting the tendency to prolapse.[6,15]

Rectal crises, called proctalgia fugax, are based on neurogenic spasm. They frequently occur during sleep, and abate spontaneously. Some obtain relief by the knee-chest position, others by sphincter dilation or enemata. The term proctalgia infantum, coined by Pounders [11] (1957), was applied only to dyschezia in allergic infants, and was described as a type of "migraine of the rectum."

The case described below appears to be a variant of sigmoidorectal intussusception in which recurrence progresses into prolapsus intussuscepti.

A one-year-old boy was observed to have an attack of pain when he screamed and motioned towards his lower abdomen and genitals. A second attack occurred two months later, a third six weeks later, and subsequent episodes almost nightly. He was usually in bed when the pain started. The pain subsided spontaneously or could be relieved by a small tap-water enema. Small amounts of blood were seen once or twice on the diaper.

Received for publication April 6, 1959.

Scripps Memorial Hospital.

At 18 months, after a barium enema was reported as normal, proctosigmoidoscopy to 25 cm. showed a large rectal ampulla into which the normal-appearing sigmoid readily descended. The patient was in lithotomy position and relaxed well.

After the studies the attacks almost vanished. A month later a symptomatic left inguinal hernia was repaired. The attacks of pain reappeared several months later and were treated conservatively.

At 3 years of age frequent attacks of lower abdominal pain brought the patient into the hospital. The pain started almost every time he lay down, day or night. The barium examination again was within normal limits. The mother stated that while giving an enema to relieve the pain she noted the enema tip touched a mass within the rectum, just inside the anal verge. When she replaced this, using a glove (as instructed), the pain was immediately relieved. There had been no vomiting and no irregularity in stools.

Because of parental anxiety and the crescendo of attacks elective surgery was recommended. This decision, after almost two years of observation and many sleepless hours for the parents, was a great relief to the family, if not to the pediatrician and the surgeon.

With a transabdominal approach the rectum and the entire left colon except the splenic flexure were mobilized. The rectum was fixed to the pelvic brim and about 1 ft. of the redundant sigmoid and descending colon was resected with end-to-end anastomosis. The descending colon was resutured to the posterolateral peritoneum.

The subsequent course was uneventful. The patient left the hospital in three days, and the attacks have not recurred in over two years since. Stools sometimes occur with some urgency, and the stool bulk is sometimes larger than before resection.

Comment

There is evidence that chronic intussusception distal to the jejunum may produce almost no symptoms of obstruction. In the absence of infarction or perforation, peritoneal irritation seems to be absent.

Megarectum and proctalgia fugax may occur on the basis of recurring acute intussusception (or prolapse) of the sigmoid. The unstable colon may actually be in segmental spasm, initially allowing it to slide into the rectum.

The surgical procedure used was essentially that described by Pemberton and Stalker (1939) with the addition of resection.[10,15] This conforms to the policy stated by Turrell [17] (1958), applying to the young, good risk patient. Resection is done to avoid kinking which might form the head of another intussusception, and to eliminate the excessive mesentery. Midline suture of the levatores ani appeared superfluous in this case, and was omitted.

Summary

Various states relating to sigmoidorectal intussusception are cited.

A case of recurrent acute sigmoidorectal intussusception and its surgical correction are reported.

We request the indulgence of authors reporting similar cases whose reports were not available to us.

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Contribution to the Problem of Kidney Transplantation in Man

J. J. GRITSMAN, M.D.; E. B. GORBOVITSKI; S. A. MUSHEGYAN, and I. M. BEREGINSKI, Moscow, U.S.S.R.

The first attempts to transplant the kidney from animal to man were made by Ullmann (1902); Jaboulay (1906), and Unger (1910) in the beginning of the 20th century. The priority in cadaver renal homoplasty in man belongs to the Soviet surgeon U. U. Voronoy (1934).

Up to the present moment all the experimental and clinical attempts to implant renal homografts have ended in failure as far as complete and permanent implantation was concerned.

The case of renal grafting from homozygous twin, described by Merrill and collaborators in 1956, is considered to be an exception.

In spite of failures the clinical need for such operations is so great, the effect of transplantation in individual cases is so striking that the number of published observations increases markedly each year.

Up to this time reports of 28 operations of this kind have been published,* though their real number is apparently much greater.

The analysis of published data indicates that renal homotransplantation in seven patients produced a pronounced clinical effect consisting of a considerable improvement of their condition.

The patients were discharged and some of them returned to work.

Taking into consideration the fact that the patients who underwent this operation had been almost hopeless, the total result is not so bad as it would seem at the first sight.

The biostimulating influence of the transplanted kidney upon the function of the recipient's affected kidneys may be of particular importance. This phenomenon was described for the first time by U. U. Voronoy in 1950. According to his observations, in cases of advanced chronic nephritis complicated with uremia (when the diuresis was poor, the specific gravity of urine low, and the kidneys were completely unable to excrete indigo carmine) the excretion of concentrated urine was observed 24 hours after the transplantation of the conserved kidney. Hence, apart from simple "unloading" of the patient's body, there has doubtless been a stimulation of the patient's own kidneys.

Consequently, the experience in renal homografting shows that this operation is absolutely justifiable because it is possible to obtain prolongation of life in hopeless cases and sometimes recovery. Side by side with these statements the valuable clinical observations are of great importance for the radical solution of the homotransplantation problem taken as a whole.

All the previous knowledge in kidney homotransplantation indicates that the experimental data obtained in animals cannot be completely transferred to the clinic. And, first of all, it concerns the periods of graft function. In animals the renal homotransplant functions 7 to 8 days on the average, while in man the satisfactory function was observed for 21 days and sometimes much longer. Besides, Oeconomos (1956) notes that filtration and tubular reabsorption may

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From the Scientific Research Institute of Experimental Surgical Apparatus and Instruments (Director: M. G. Ananiev) and Town Hospital No. 40 (Physician in Chief: J. S. Shipatovski).

* See summarizing table in Joekes, Porter, and Dempster's study (1957).[10]

remain on sufficiently high level. The operation which can give a patient this essential help is surely quite permissible.

Indications for the Operation

The homotransplantation of a kidney has been performed in patients with various diseases: trauma of a single kidney, nephropolycystosis, acute necrotic nephrosonephritis, corrosive sublimate intoxication, nephrosclerosis in hypertension, and so on. Analysis of the whole experience of kidney transplantation indicates that, before the solution of the incompatibility problem as a whole, kidney transplantation may be performed mainly as a temporary measure for the patient's "unloading" and possibly for stimulating the recovery of the recipient's own kidneys.

This operation must be employed as the last attempt to save the life of a patient when all the usual treatments have already been tried and the patient's condition still permits performance of the operation. In cases when the patient's own kidneys are unable to resume their function, the transplantation will prolong the life of a patient and reduce his suffering. Considering the above statement, supported by other surgeons' data represented in detail in the literature and by our own knowledge in the field of experimental renal homotransplantation, we have twice performed this operation to save the life of our patients.

We believe that the complexity of the problem and its actuality require that every new effort to save the patient with the help of renal homotransplantation should be published, whatever is the final result of the operation.

The first of our operations was performed on Sept. 10, 1954, in Kalinin Regional Hospital (J. J. Gritsman with the assistance of A. G. Karavanov and I. F. Kobelev). The second was performed by us on April 14, 1956, in Hospital No. 40 in Moscow.

Case 1.—The first patient, a 28-year-old man, was admitted to the hospital on the third day of complete anuria, which had suddenly developed after a chilling. The diagnosis was "acute necrotic nephrosis." Some therapeutic measures, including lumbar procaine (Novocain) hydrochloride block and ureteral catheterization ended in failure. Uremia was increasing. In this connection the next day bilateral renal decapsulation was performed (M. P. Voskresenski) and a biopsy specimen was taken. The histological examination revealed acute glomerular nephritis. During the following days, in spite of energetic treatment, anuria remained and uremia increased. Nonprotein nitrogen reached the level of 175 mg. %, the increase during the last 24 hours being 43.4 mg. %. Therefore it was decided to transplant the cadaver kidney, and this was done on the seventh day of complete anuria. The kidney was taken from the cadaver of a boy of blood group II (A) (the patient's blood group was III [B]) five hours after sudden death and was kept in isotonic saline solution with penicillin at temperature 6 C for 24 hours.

The transplant was placed under the skin of the left thigh. First of all the anastomosis between the femoral and renal arteries was made, and the kidney was perfused by the recipient's blood; after that the veins were sutured. The anastomoses were

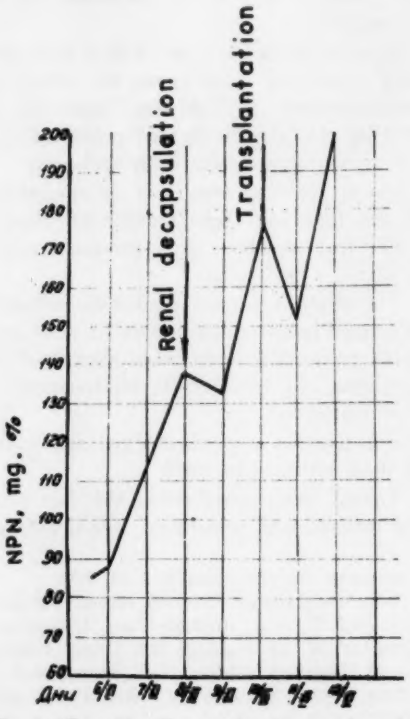

Fig. 1 (Case 1).—Nonprotein nitrogen dynamics.

carried out according to Carrel's method. In 20 minutes the excretion of a few drops of turbid urine began from the ureteral orifice. Within the next few days the patient's condition was not worse. During 24 hours nonprotein nitrogen decreased to 151.2 mg. %, i. e., there was 24 mg. % reduction (Fig. 1).

After 36 hours urinary excretion ceased; nonprotein nitrogen markedly increased, and the patient died a few hours later. The autopsy revealed irreversible changes in the patient's own kidneys and venous thrombosis of the renal transplant with circulatory disturbances in its parenchyma.

CASE 2.—The second patient, a 53-year-old woman, was admitted to the hospital with the diagnosis: "Intoxication with unknown poison." She complained of weakness and nausea, from the morning till the time of admission she didn't urinate. Nonprotein nitrogen on admission was 123 mg. %. Within the next few days, in spite of treatment, the patient's state became gradually worse. Urination was absent. Procaine hydrochloride block, ureteral catheterization, and medication were without result. In this connection bilateral decapsulation was undertaken on the fifth day of the anuria, but the patient's condition was not improved. The next day after the operation NPN was 141 mg. %.

The anuria being still in progress, on the seventh day it was decided to undertake the homotransplantation of a kidney. The operation was performed in the same way as in the first case, but the vessels were connected with the help of the vessel suture apparatus (Scientific Research Institute of Experimental Surgical Apparatus and Instruments). The kidney was taken from a 19-year-old youth of blood group I(O), who died of trauma (the patient being of blood group II [A]) four and a half hours after death and placed in isotonic saline solution with penicillin. The kidney was transplanted three hours after its removal. There was a vascular anomaly—the presence of two renal arteries. One of them was ligated, the anastomosis being made between the other and the femoral artery.

Before transplantation the kidney was perfused with 500 cc. of Ringer solution. Seven minutes after the completion of the anastomosis of the vessels the drop excretion of transparent liquid began. Next day it was possible to collect a small quantity of urine from the transplanted kidney. The turbid urine contained 49.5% protein and fresh red blood cells. During the following 24 hours we were able to collect about 10 cc. of urine with blood from the ureteral orifice of the transplanted kidney. The bladder catheterization gave 100 cc. of turbid urine with blood (Fig. 2). NPN was about 145 mg. %.

Toward the end of the second day the transplanted kidney ceased to function. The patient's condition after a slight stabilization gradually worsened. On the fifth day the kidney was removed

Blood—Biochemical Data (Case 2)

Date	NPN, Mg. %	Indican, Mg. %	Note
4/10	123	0.4	
4/11	123	0.4	
4/13	141	—	
4/14	146 *	—	Renal grafting performed
4/16	144	0.8	

* The test was performed before the transplantation.

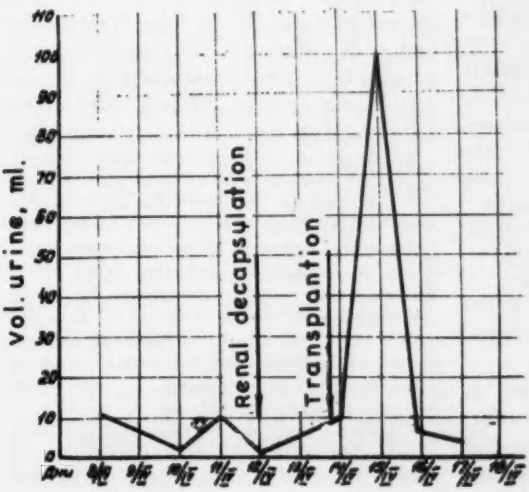

Fig. 2 (Case 2).—Urinary output of patient's own kidneys.

and was found considerably enlarged. The anastomosis between the renal and femoral arteries was found to be intact, but the venous return was insufficient.

Microscopy of the kidney revealed necrosis and autolysis. The patient died five days after the operation. The autopsy revealed total necrosis of both her own kidneys.

From the case histories just discussed it appears that we doubtless had positive, though temporary, effect in two patients. The unsuccessful final result was due mainly to the fact that both our patients had irreversible changes in their own kidneys. This we surely could not know before the operation.

The data in the literature, and our own experimental and not great clinical practice indicate that the operation of renal transplantation has its peculiarities from the surgical point of view, which must be discussed briefly.

General Requirements for the Operation of Renal Homotransplantation

As long as the transplantation is first of all a vessel operation, from the surgical point of view, the surgeon starting it must well master the vessel suture technique. The majority of surgeons use Carrel's suture. Experiments show that better results may be obtained by use of the vessel suture apparatus, which considerably reduces the time of operation and markedly decreases the incidence of postoperative thromboses. Careful attention to asepsis is of particular importance in this kind of operation because the circulatory insufficiency which develops frequently to some degree creates the substratum for suppuration, and this results in thrombosis and loss of a transplant.

Choice of Site for the Graft

The kidneys have been transplanted into the elbow fossa, lumbar region, iliac fossa, renal fossa, and into the thigh.

The sites most generally used are as follows: (1) transplantation in the lumbar region, the renal artery being connected end to end to one of the iliac artery branches and the vein end to side to common iliac vein with the ureter implanted into the bladder; (2) transplantation in the thigh, the renal artery being connected end to end to the femoral artery distal to the deep femoral artery origin and the renal vein to the femoral vein. The ureter is placed upon the skin.

The last method is probably the best one in the majority of cases for the following reasons:

1. It is preferable to perform the least traumatic operation when the patient's condition is grave. The transplantation into the thigh is quicker and easier than that into the iliac fossa or lumbar region.

2. The end-to-end anastomosis permits use of the vessel suturing apparatus, the advantages of which have been already mentioned.

3. The patient tolerates local anesthesia better; this is very important because additional intoxication is undesirable when the patient is in a grave condition.

4. It is possible to have the kidney and its function under constant and direct control.

5. It is easy to observe and take care of the ureteral orifice.

6. The removal of the kidney when its function stops may be performed in a few minutes.

In both our cases we have used the renal transplantation into the thigh under local anesthesia.

Compatibility

Without dwelling on the question of tissue compatibility, which is discussed in detail in the literature, (N. N. Jukov-Veregenikov and P. N. Kosjakov 1957) we believe that practically in renal transplantation in man one should consider the possibility of the following measures to reduce incompatibility.

1. Selection of a donor most closely approximating the recipient as far as blood group antigens are concerned, for example. But such selection when cadaver material is used for the transplantation is very difficult; this has been distinctly indicated in Kosjakov's report. One should seek to transplant organs of the same group. But side by side with this we may note that so far as a temporary renal grafting is concerned the operation should not be disregarded in emergency cases because of the lack of congruity of the antigen structure of donor and recipient.

2. Influence upon the recipient with a view to reducing his immunologic reactivity. For this purpose some authors (Küss and others, 1951) admin-

ister the adrenocorticotropic hormone corticotropin (ACTH). Other investigators (Dubost and others, 1951) have combined corticotropin with cortisone. In both cases there was no marked result, however. Use of antihistaminic drugs was not successful either. Doubtless, research in this direction must be continued.

3. Isolation of the renal transplant from the recipient's tissues with a view to reducing their contact. It may be performed by placing the kidney in a plastic sack.

4. Organ conservation. It is believed not without reason that conservation may reduce to some degree the antigen activity of the transplant. This problem also requires further special study.

As to perfusion of a transplant, the available data do not allow one to draw conclusions as to the advisability of this measure, because both in experiment and in the clinic prolonged function of perfused and nonperfused transplants has been found (A. G. Lapshinski, E. B. Gorbovitski, G. V. Medvedeva, and S. A. Perestoronin, 1957). It is to be noted that according to the general conception of the immunological nature of incompatibility in homoplasty, one may hope that the removal by perfusion of proteins in solution in the transplant blood would reduce to some extent the recipient's reaction to the graft.

Duration of the Period of Circulatory Interruption

With the exception of U. U. Voronoy, who transplanted the kidneys after 12-28 days of conservation, the average period of the circulatory interruption varies from 14 minutes to 6 hours according to some authors' reports. The interruption of the circulation for six hours and longer does not probably result in the loss of a transplant. Moreover, it seems that a two- to three-hour interval in circulation may have a beneficial influence upon the duration of function of a transplanted kidney.

It is necessary to note, however, that a prolonged interruption in the circulation may lead to postoperative anuria, which sometimes continues in experiments from 18 to 30 days (A. G. Lapshinski, E. B. Gorbovitski, G. V. Medvedeva, and others, 1957), and according to Hume's data goes on for 19 days, as far as renal transplantation in man is concerned.

The problem of employment of the artificial kidney is of particular interest. Some surgeons suppose that the use of this apparatus would eliminate the necessity of an organ transplantation as a temporary therapeutic measure. But a number of doctors who have the artificial kidney at their disposal and use it widely do not give up their attempts to transplant the kidney, the apparatus being applied sometimes to prepare a patient for the operation (Merrill and others, 1956).

The following reasons are given for such procedures:

1. The artificial kidney, which reproduces only the renal filtration, cannot substitute all the functional multiformity of a living organ. Therefore, when the operation is successful, one obtains more complete effect than by using the apparatus.

2. When the artificial kidney is used there is no biostimulating influence upon the recipient's own kidneys. This fact formed the basic principle of U. U. Voronoy's operations.

3. In some cases after the transplantation it has been possible to obtain a continuous and satisfactory function of the transplanted kidney for five and a half months (Hume and collaborators, 1955), that being unattainable by use of modern apparatus.

4. The conditions for use of the artificial kidney are more complicated and require more detailed laboratory observation than the operation.

The above does not mean that we oppose one method to the other. Probably they should supplement each other.

Data from literature referred to above and our own small experience lead us to believe that the operation of kidney transplantation must find its place in systematic contrauremic treatment.

The operation must be done in strictly selected cases, the appropriate equipment being available. Every case has to be analyzed in detail because it gives concrete scientific data the accumulation of which is necessary for the solution of the problem of organ transplantation.

Scientific Research Institute of Experimental Surgical Apparatus and Instruments.

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Palmar Lipoma

Report of a Case

EUGENE T. McENERY Jr., M.D.; ROBERT L. SCHMITZ, M.D., and PETER A. NELSON, M.D., Chicago

In 1957 one of us (RLS) with Keeley reported a series of four lipomas of the hand, three in the palm, and one in the finger. At that time only 14 palmar lipomas had been reported; our 3 brought the total to 17. We were unable to ascertain the number of digital lipomas reported but it was equally small or smaller. Since then no further cases have been recorded in the literature. Therefore, we think it is appropriate to report a recent case of ours which involved a finger as well as the palm and in which the diagnosis was correctly established preoperatively with the help of roentgenograms, a diagnostic aid which has not previously been mentioned in this regard.

Submitted for publication April 10, 1959.

Surgical Resident, Mercy Hospital (Dr. McEnery). Associate Clinical Professors of Surgery, Stritch School of Medicine of Loyola University, and Senior Surgeons, Mercy Hospital (Drs. Schmitz and Nelson).

An 86-year-old Negro came to Mercy Hospital Free Dispensary in August, 1958, because of a mass in the palm of his right hand. He said that the mass had been present about 25 years and had slowly enlarged during that time; it was asymptomatic. On examination a mass about 5 cm. in diameter was located in the distal, central palm and base of the ring finger, especially along its radial side (Fig. 1). There was a Dupuytren's contraction of the palmar fascia at the central edge of the lipoma, and the ring finger was carried in 20-degree flexion. The mass felt cystic, was nontender and seemed to transilluminate with strong light. There was hypesthesia over the palmar surface of the ring finger. The possibility of lipoma was included in the diagnosis, along with ganglion.

Roentgenograms were made of the hand and demonstrated a relative translucency of the tissue of the mass compared with the surrounding soft tissues (Fig. 2); a diagnosis of lipoma was reported.

Under general anesthesia (thiopental [Pentothal]-ether-nitrous oxide), with a tourniquet applied to the arm just above the elbow, an incision, 3 cm. long, was made along the ventral-radial

Fig. 1.—Swelling of distal central palm and base of ring finger from lipoma. Note Dupuytren's contracture at central edge of lipoma.

Fig. 2.—Roentgenograms showing radiolucency of lipoma compared with other soft tissues.

Fig. 3.—The gross specimen. Note the prolongation which entered the lumbrical canal.

border of the proximal phalanx and the web of the ring finger. The lipomatous mass was well encapsulated; it pushed the digital nerve and vessels dorsally; a prolongation entered the corresponding lumbrical canal; the tumor was removed without incident. Considerable dead space remained, so a short, multifenestrated, 15-gauge, polyethylene tube was placed through the dorsal side of the web, and suction was applied to it for 72 hours. The postoperative course was uneventful. The wound healed by primary intention.

The specimen measured 4.5×4×1 cm. (Fig. 3). The pathological report was lipoma.

Comment

Lipomas of the palm or finger are unusual; they feel cystic when palpated. For these reasons the diagnosis is often missed preoperatively; instead a diagnosis of ganglion is made. In our case, roentgenograms were so characteristic of lipoma that they helped to establish the correct diagnosis.

Summary

The 18th palmar lipoma to be recorded is described.

55 E. Washington St. (2) (Dr. Schmitz).

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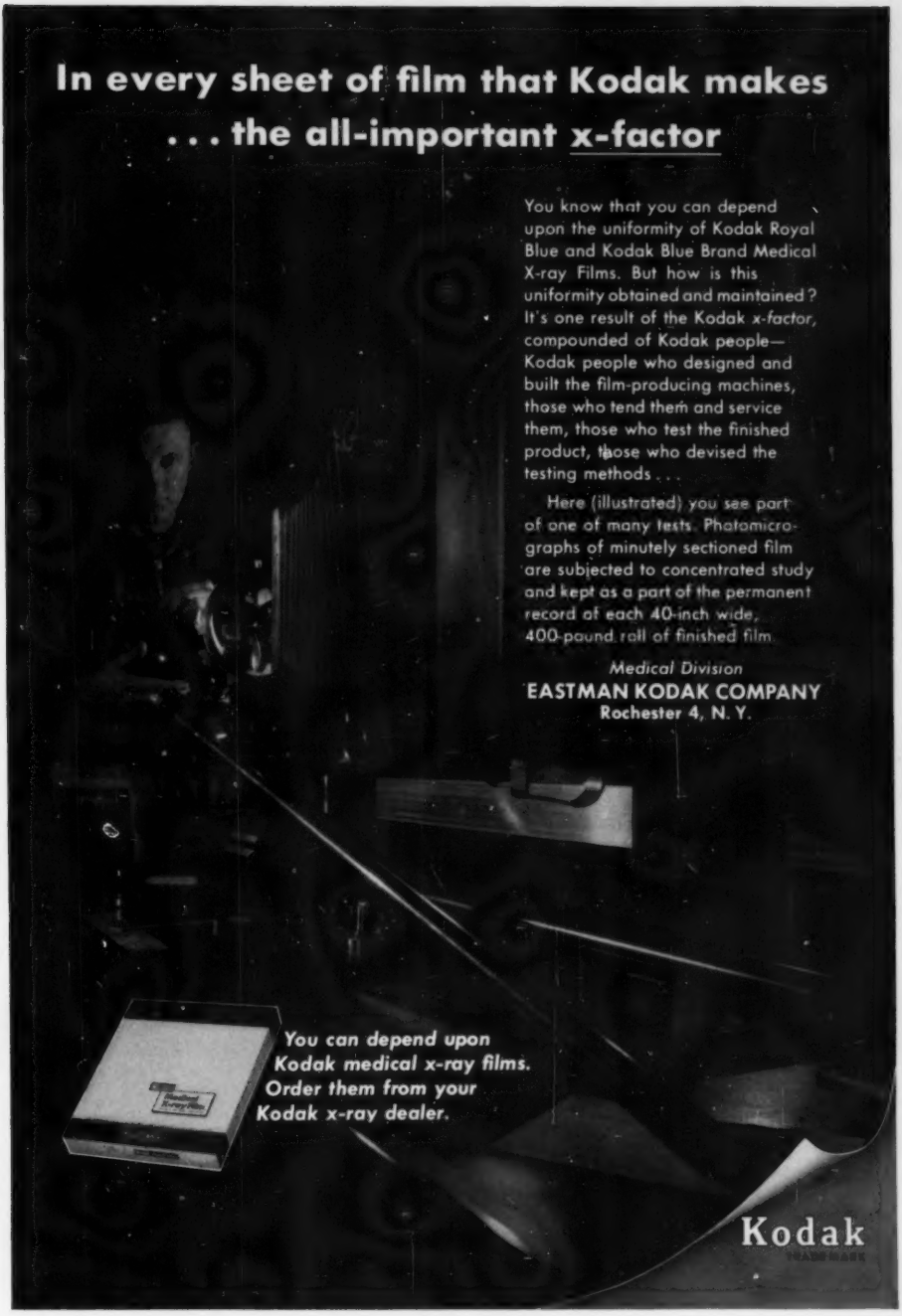

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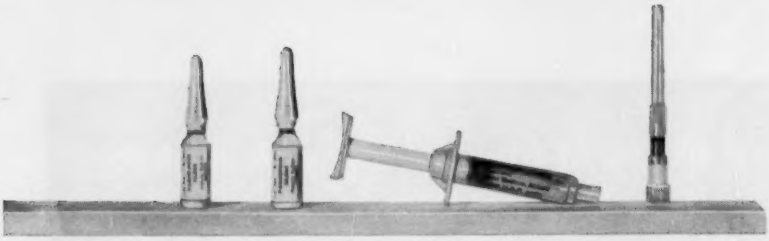

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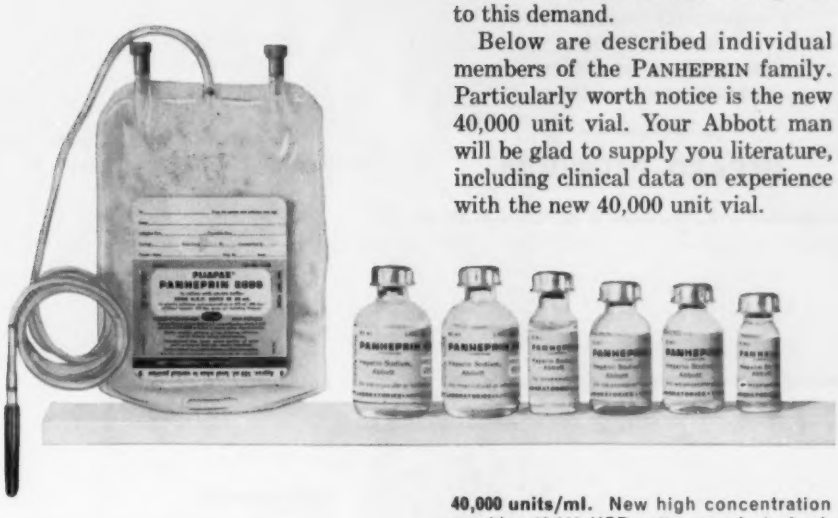

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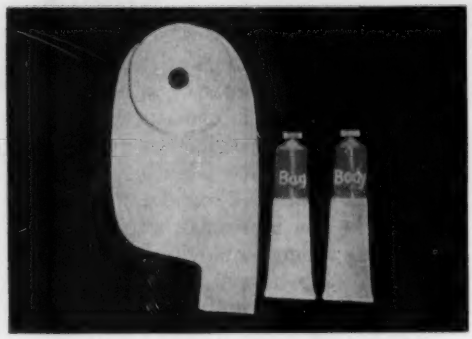

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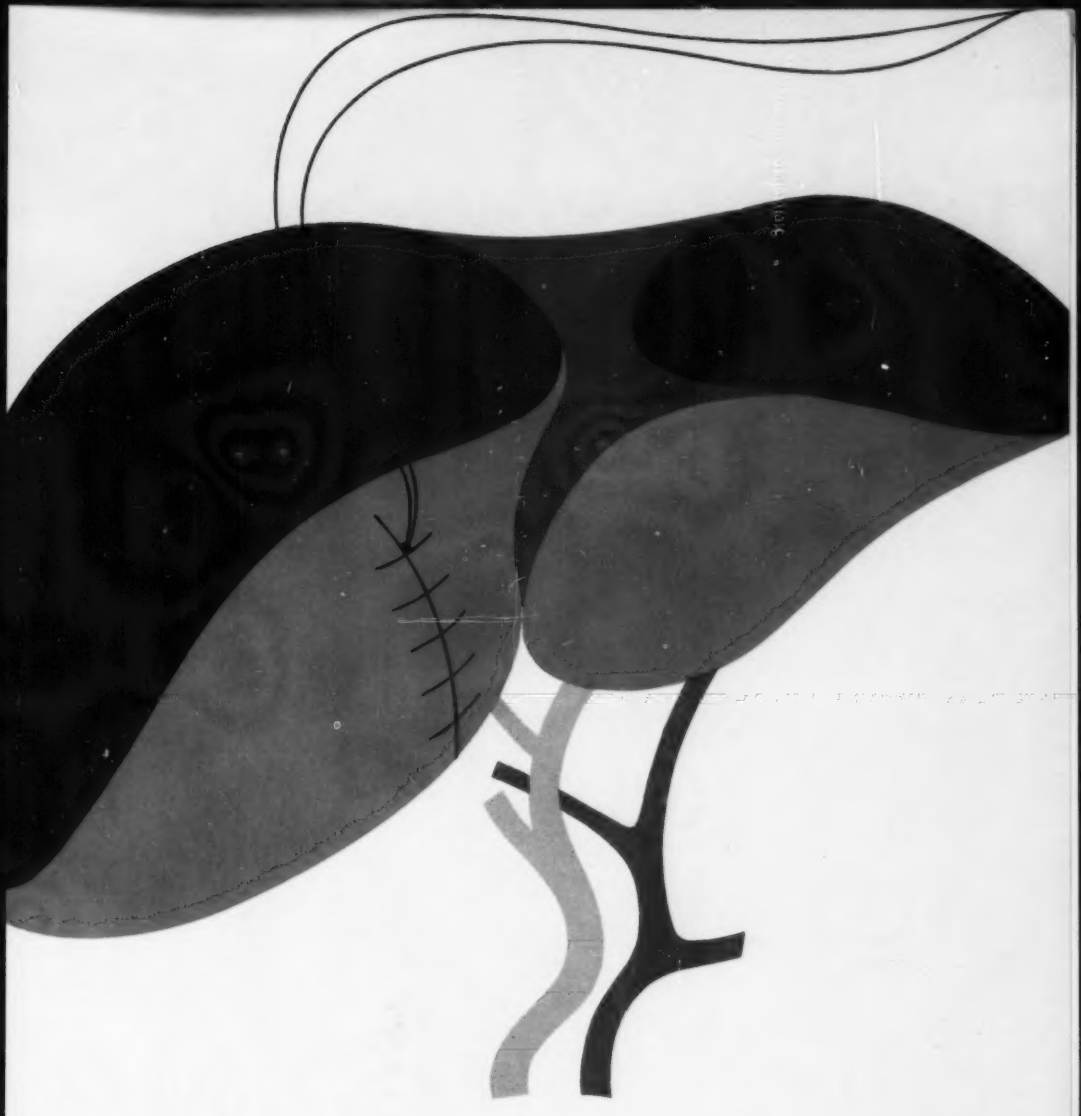

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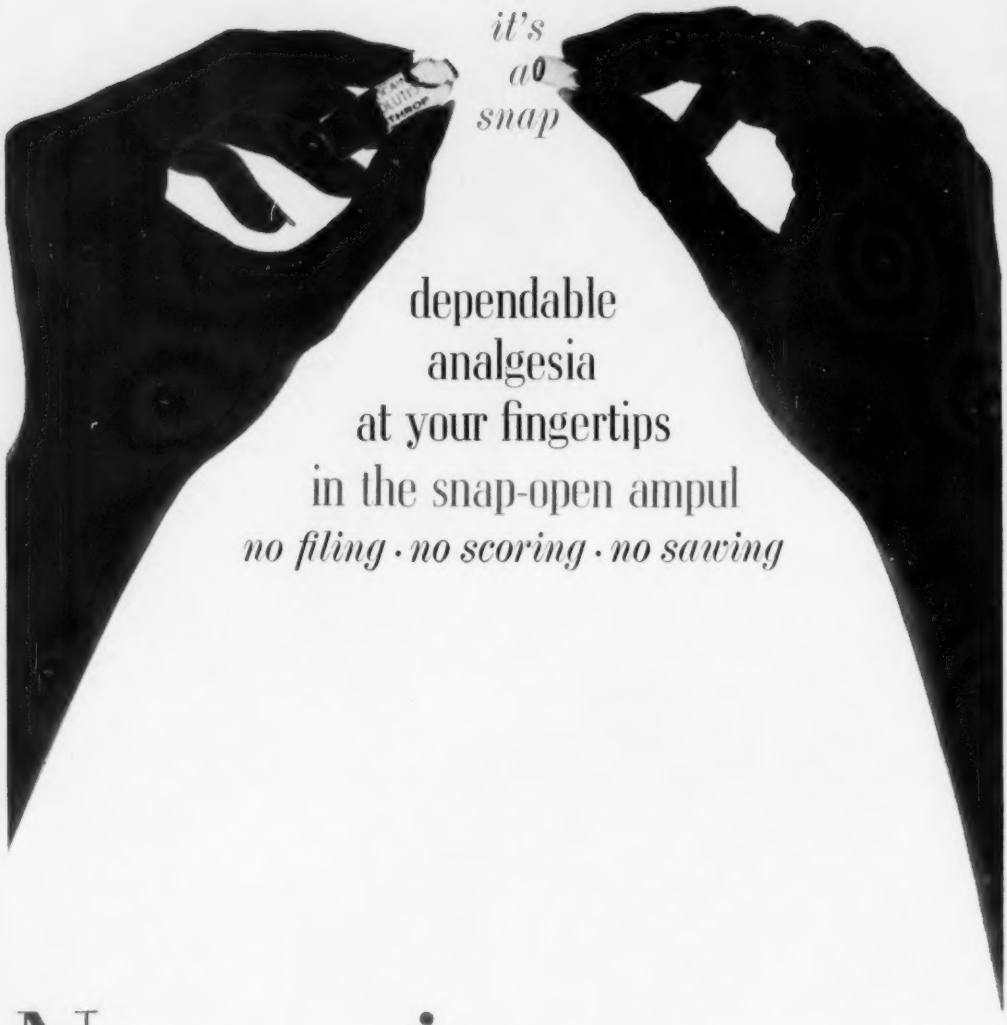

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